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SECTION OF BIOLOGICAL AND MEDICAL SCIENCES

THE USE OF PARTICLE-BEARING *PARAMECIUM* IN SCREENING FOR POTENTIAL ANTITUMOR AGENTS*

Anthony T. Soldo

Biological Research Division, Schering Corporation, Bloomfield, N.J.

Introduction

The animal microorganism *Paramecium*, a member of the phylum Protozoa, may provide a unique system for the study of substances that are selective in their action (that is, antitumor agents). Certain stocks of these organisms contain in their cytoplasm hundreds and even thousands of particles designated as kappa, lambda, mu, and pi.[1] Essentially hereditary endosymbiotes, these particles appear to be capable of undergoing mutation and self-reproduction. Interference with their reproduction by means of chemical agents without injury to the host may indicate a degree of selectivity on the part of the agent tested. Using kappa-bearing paramecia in bacterized medium, for example, Stock *et al.*[2-4] found that 2,6-diaminopurine was the only one of a number of purines and pyrimidines tested that actively reduced the kappa content of the cells.

The purpose in undertaking the work reported here was twofold: (1) to re-examine this and other particle-bearing systems of *Paramecium* under bacteria-free conditions with the aim of developing a model for the study of host-symbiote relationships; and (2) to test the application of such a system to screening for agents potentially differential in their action. What follows is a brief account of the development of an axenic medium for a number of particle-bearing paramecia and the results of a more detailed study of a particular strain, *Paramecium aurelia*, stock 299χ.[5]

Axenic Culture

Representative particle-bearing strains of *Paramecium* were freed from contaminating bacteria (that served as a source of food for the protozoans) and placed in sterile culture media of varied composition.[6] In this

*This paper, illustrated with slides, was presented at a meeting of the Section on May 8, 1961. The work described in this article was supported in part by a government contract SA-43-ph-1929 to the Cancer Chemotherapy National Service Center, National Cancer Institute, Public Health Service, Bethesda, Md.

The Section of Geological Sciences held a meeting on May 1, 1961, at which J. E. Upson of the United States Geological Survey, Mineola, N.Y., presented a paper entitled "Buried Bedrock Valleys on the New England Coast." This paper will be published in the November 1961 issue of the *Transactions*.

The Section of Chemical Sciences held a meeting on May 2, 1961, at which D. F. Bradley of the National Institute of Mental Health, Public Health Service, Bethesda, Md., presented a paper entitled "The Molecular Biophysics of Dye-Polymer Complexes." No manuscript has been received.

The Division of Mathematics held a meeting on May 3, 1961, at which Saunders MacLane of the University of Chicago, Chicago, Ill., presented a paper entitled "Recent Progress in Finite Group Theory." No manuscript has been received.

manner, a suitable axenic medium (medium free of all living forms except the particle-bearing paramecia) was developed that supported the growth of the protozoans and the maintenance of the particles for the following stocks of *P. aurelia* 51κ, 299λ, 138μ, and 139π (TABLE 1). The lambda-bearing strain (stock 299λ) was selected for further study because it offered certain technical advantages (for example, lambda particles are larger than the kappas and may be more easily seen in stained preparations) and for the ease with which these animals could be cultivated axenically.

TABLE 1
COMPOSITION OF AXENIC MEDIUM

Vitamins	μg/ml.	Salts	μg/ml.
Ca Panthothenate	2.5	$MgSO_4 \cdot 7H_2O$	25.0
Nicotinamide	2.5	$Fe(NH_4)_2(SO_4)\ 6H_2O$	6.25
Pyridoxal HCl	2.5	$MnCl_2 \cdot 4H_2O$	0.125
Riboflavin	2.5	$ZnCl_2$	0.015
Folic acid	1.25	$CaCl_2 \cdot 2H_2O$	12.5
Thiamine HCl	7.5	$CuCl_2 \cdot 2H_2O$	1.25
Biotin	0.625 mμg	$FeCl_3 \cdot 6H_2O$	0.31
Stigmasterol	0.2	K_2HPO_4	250.0
		KH_2PO_4	250.0
Proteose peptone	5.0 mgm	EDTA	5.0
Edamine S	10.0 mg		
NDF (yeast fraction)	5.0 mgm		

The Lambda System

In axenic medium, animals of stock 299λ were found to contain an average of approximately 500 rod-shaped, self-duplicating bodies ranging in size from 1μ dia. × 3-6μ and distributed at random throughout the cytoplasm. Particles freed from paramecia by mechanical disruption of the cells were negative to Gram's stain and, after treatment with acridine orange, appeared bright red when viewed in UV under dark-field illumination. It was possible to visualize lambda within the cells with nuclear stains such as Giemsa and acetoorcein. Cellular particles stained weakly if at all with Feulgen and, after treatment with the enzyme ribonuclease, stainability with nuclear stains was lost. (R. Tanquay, personal communication). These results indicate the presence of ribonucleic acid in the particles and little, if any, deoxyribonucleic acid. This contrasts with the situation found with the kappas that contain DNA.

A remarkable synchrony was found to exist between the lambda population and the population of the protozoans. This situation became apparent when the increase in *total* population of lambda (that is, average lambda per cell × protozoan population density) was compared with the increase of the protozoan population during the course of a typical growth

cycle (FIGURE 1). The lambdas appear to behave as a distinct population distributed randomly throughout the collective cytoplasm of the protozoan host. It would seem that division of lambda is synchronized to processes that are associated with the protozoan population rather than the protozoan itself.

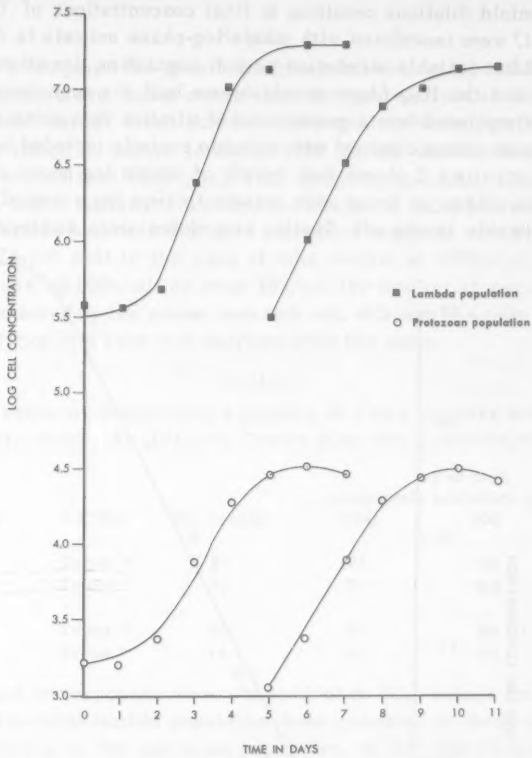

FIGURE 1. Comparison of increase of total lambda with protozoan.

Assay Procedures

Two criteria for assessing activity of test agents were employed: (1) inhibition of growth of the protozoan population without regard to effect upon lambda and; (2) selective inhibition of the lambdas themselves. Numerical estimates of protozoan population densities satisfied the conditions set forth in the first criterion. The attempt to define quantitative criteria for the second measure of activity—that is, substances that selectively interfere with the reproduction of lambda—led initially to a comparison of the average number of lambdas per cell of experimentals with those of the control. Averages thus obtained varied

within wide limits and difficulties in reproducing results were encountered. These difficulties were overcome when values for total *lambda*, obtained by multiplying the average lambda per cell by the protozoan population density, were used.

Replicate volumes of culture medium containing test substances in serial, tenfold dilutions resulting in final concentrations of 0.1 γ/ml to 1000 γ/ml.[7] were inoculated with single log-phase animals in depression slides.[7] After suitable incubation period, population densities were determined and the ID_{50} (dose at which one half the organisms were inhibited) interpolated from a graphic plot of titration data, using as maximal growth those values obtained with suitable controls included in the same titration. FIGURE 2 shows that growth of single log-phase animals in depression slides is linear with respect to time for a period of 8 days and afterwards levels off. Similar procedures were employed for test

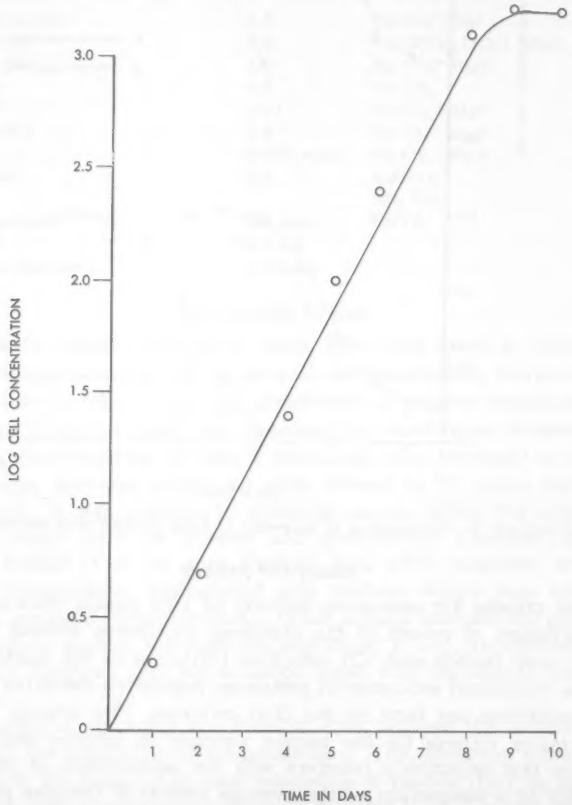

FIGURE 2. Single cell growth curve in depression slide culture.

substances assayed in tube culture. Incubation was carried out for a period of 6 days at 27° C.—the time required to reach maximum population density. Substances screened were those selected from the list of CCNSC* compounds presently employed for the evaluation of test-screening procedures.

Results

TABLE 2 compares the growth inhibitory activity in tube and depression slide culture with tumor active and inactive materials as determined by the CCNSC animal tumor screen. Approximately three fourths of the substances listed as active in the CCNSC screen were active against *P. aurelia* at less than 1000 γ/ml. This compares favorably with results obtained in tissue culture.[8] However, the number of false positives—that is, tumor inactive materials that give a positive response with *P. aurelia*, was high—76 per cent in the case of tube culture at 1000γ/ml. At test concentrations of 100γ/ml. or even 10γ/ml. the number of tumor active materials detected by the screen was reduced, although the ratio of tumor actives to tumor inactives was approximately the same.

TABLE 2

COMPARISON OF INHIBITORY ACTIVITY IN TUBE AND DEPRESSION WITH TUMOR ACTIVE AND TUMOR INACTIVE COMPOUNDS

Culture	CCNSC	No. tested	Per cent compounds inhibitory (μg./ml.) 1000	100	10
Tube	Tumor +	27	74	56	16
	Tumor −	37	76	42	22
Depression	Tumor +	20	80	40	15
	Tumor −	18	67	55	11

Two types of responses were obtained when ID_{50} values for the inhibition of the total lambda population were compared to those obtained for the inhibition of the protozoan population. In the first (FIGURE 3), no significant differences between these values were found. FIGURE 4 illustrates the second type of response in which a greater inhibitory effect was observed for the lambda population than for the protozoan population. Substances causing a relative increase in the lambda population were not found. Apparently the particles are dependent upon one or more vital processes of the cell (or cellular population) which, when inhibited or inactivated as a result of exposure to test substances, prevent the lambdas from dividing.

A kind of therapeutic index is obtained when the ratios of the ID_{50} values for the protozoan and the lambda (P/λ) are compared. Quantitative expression of the relative activity of test substances may thus be

*Cancer Chemotherapy National Service Center, Washington, D.C.

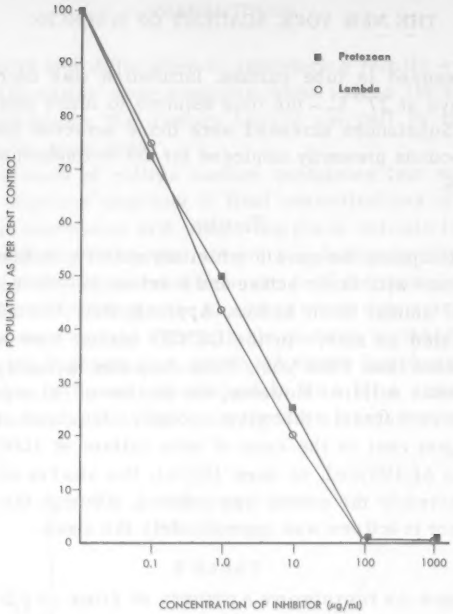

FIGURE 3. Growth inhibition with substituted 1,2-dihydro-s-triazine.

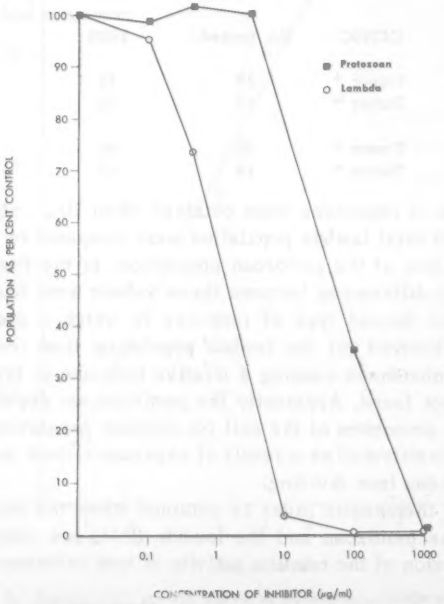

FIGURE 4. Growth inhibition with 1-aminocyclopentane-1-carboxylic acid.

achieved. TABLE 3 illustrates the results of a series of trials using streptomycin, a substance that causes reduction of lambda. Variation in P/λ values noted here was a function of the relative inaccuracy with which the end points were determined. A greater degree of accuracy could be achieved by selecting test concentrations over a narrower range of values.

TABLE 3

SELECTIVE INHIBITION OF LAMBDA WITH STREPTOMYCIN

Trial no.	ID_{50} (μg./mL.) *Paramecium*	Lambda	Ratio P/λ
1	370	300	1.23
2	200	102	1.96
3	350	180	1.94
4	320	250	1.24
Average	310 ± 54	208 ± 67	1.59 ± 0.36

TABLE 4 lists 12 substances of a total of 102 tested that were found to reduce lambda significantly in this system. Two features of these results are notable: (1) the variety and type of substances detected and; (2) the apparent lack of correlation between ID_{50} values obtained for the protozoans and the P/λ ratio.

TABLE 4

SUBSTANCES SELECTIVELY INHIBITORY FOR LAMBDA

Compound	*Paramecium* ID_{50} (μg./mL.)	Lambda	Ratio (Pλ)
2-amino-5-nitrothiazole	62	5	12
1,4-dinitropiperazine	>1000	600	>1.6
p-fluoroaniline	34	2	17
Benzenesulfonic acid hydrazide	60	4	15
Sarcolysin	>1000	175	>5.7
1-aminocyclopentane-1-carboxylic acid	90	3	30
deoxypyridoxine HCl	>1000	140	>7.1
4,6-diamino-1-(*m*-chlorophenyl)-2-hexyl-1,2-dihydro-s-triazine HCl	15	3	5
1-Methyl-4-n-propylaminopyrazolo-(3,4-d)-pyrimidine	14	3	5
Hydroxy urea	250	6	41
Cytoxan	400	240	1.7
Streptomycin	350	200	1.8

Four of the substances on the list, sarcolysin, 1-aminocyclopentane-1-carboxylic acid, deoxypyridoxine HCl and cytoxan were active in the CCNSC animal tumor screen. Both cytoxan and 1-aminocyclopentane-1-carboxylic acid have undergone clinical trials, the former for the treatment of human leukemias and related cancers[9] and the latter for the

treatment of multiple myeloma.[10] Sarcolysin has been used to treat some solid tumors in man.[11]

Discussion

The presence of lambda particles in the cytoplasm of its protozoan host and the attempt to use this system to predict whether substances are selective in their action raises a number of questions. Two are most pertinent. What is the nature of the particles? Is it possible for an animal microorganism, phytogenetically remote, to serve as a host-tumor system?

Superficially the particles resemble bacteria. They are of the proper size and are similar morphologically as well as in staining characteristics. The observed behavior of lambda as a discreet population and the susceptibility of the particles to antibiotics (streptomycin) support this view. Critical students may want more decisive evidence: that is, extracellular cultivation of the particles and the demonstration of intraparticle enzymes (now experimentally feasible as a result of axenic cultivation). From the standpoint of practical interpretation, the particles may be considered to be bacterial endosymbiotes well adapted to their cytoplasmic residence. In effect, lambda-bearing paramecia provide us with test-tube model of a host-parasite system which, possessing the advantages of an *in vivo* system, may be studied in a controlled sterile environment.

The fundamental unity of biochemistry argues in favor of using the lambda system to detect substances that may be selective in their action. Indeed, several have been found (TABLE 4). Unlike bacteria which have been used as models for a wide range of investigations, *P. aurelia* is an animal organism. Even from the nutritional standpoint, growth requirements for this and similar species rival and exceed that of man.[12,13] Certainly the degree to which the lambdas have incorporated themselves into the economy of the host offers the possibility that this intimate relationship may mimic subtle differences that must exist between normal and tumor cells.

Similar enzymatic machinery may be present in both mammalian and protozoan cells. Activity of cytoxan in the lambda system is an interesting case in point. Recent evidence[14] indicates that this substance, a derivative of nitrogen mustard, is activated by enzymes present in cells of rat liver. It is postulated that this is accomplished by phosphoamidases present in this tissue which split the P-N bond and release the alkylating agent. *Paramecium* (or lambda) may possess similar enzymes.

The lambdas contain RNA (although its distribution in the particle is unknown) and little or no DNA. Other strains of *Paramecium* harbor smaller self-reproducing cytoplasmic particles, the kappas, mu's and pi's which on the basis of their stainability with Feulgen, contain DNA. These organisms, for which an axenic medium is now available, would provide additional host-parasite systems for study. Hopefully, even more

unique responsiveness to test substances will be found with these systems.

Acknowledgments

I express my sincere appreciation to Rae C. Woods and William E. Ronca for their competent technical assistance.

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DIVISION OF OCEANOGRAPHY AND METEOROLOGY

OCEAN AND SEA–ICE RESEARCH IN THE ARCTIC OCEAN VIA SUBMARINE*

Waldo Lyon

United States Navy Electronics Laboratory, San Diego, Calif.

Introduction

The capability of submarines to navigate under sea ice became public knowledge with explosive suddenness when news of the polar crossing by the U.S.S. *Nautilus* was released in August 1958. The stories of the first under-ice expeditions to the North Pole by submarines *Nautilus* and Skate have been skillfully told by their two commanding officers, William R. Anderson (1959) and James F Calvert (1960), respectively.

The first successful dive was made August 1, 1947 under sea ice in the Chuckchi Sea. Scanning sonar and visual observation by periscope was used to guide the U.S.S. *Boarfish* from open water under the ice fields for a distance of 3 miles and out again to open water. Many experiments followed each succeeding year, using Fleet type, diesel-battery submarines to develop diving and sonar techniques under ice and using ice-breakers to conduct oceanographic and bathymetric surveys of unknown areas. In 1957, when nuclear power became available the *Nautilus* cruised 1300 miles under ice, and the Arctic Ocean was truly opened to rapid exploration. The intent of this paper is not to retell the story of the many expeditions but rather to show how a submarine operates under sea ice and how it can be used as a research tool for the study of ocean-cryology.

To the submariner, the ice covering the sea appears to be a canopy over his ship, and is called the sea-ice canopy. During summer, the canopy is a drifting, fragmented collection of melting pieces of ice that have all possible sizes, shapes, and thicknesses: for example, large flat areas 5 to 12 ft. thick, or old pressure ridges where the ice sheet had broken and stacked in great, jumbled heaps to a thickness of 30 ft., or more, possibly to 130 ft. Similarly, the open water spaces between ice floes have all sizes and shapes; total coverage of open water is, perhaps, 5 per cent. Many open water spaces (polynya) are sufficiently large for a submarine to surface without contacting ice. During winter, the old summer ice is cemented together by new sea ice into a contiguous ice canopy. Under wind stress, zones of compression and tension develop within the canopy, producing pressure ridges in compression and great cracks, or leads, in tension. These cracks are of particular interest to the submariner because open water is exposed, which under the winter

* This paper, illustrated with slides, was presented at a meeting of the Division on May 9, 1961.

ambient air temperature will be quickly covered with new sea ice. For example, with air temperature of -40° C., 1–inch-thick growth is expected within a few hours, perhaps increasing to 1 foot within the week, and to 3 feet within the month. The rate of growth of sea ice is dependent on many factors: water temperature, salinity, air temperature, wind, cloud cover, and snow fall (E.B. Callaway, 1954). Many heat budget, ice growth studies have been made or are still in progress to evaluate the many factors. The thin spots, of a thickness of 3 feet or less, that form in the canopy, are called ice skylites because by periscope they look like heavy, green, translucent glass panels in the canopy.

There are six characteristic situations in which the submarine is required to operate, namely; (1) under minimum ice cover (summer, 5 per cent open water); submarine may surface in open water; (2) under maximum ice cover (winter–spring, 0 per cent open water); submarine must break through ice in deep water; (3) during maximum dark period (zero direct sunlight or twilight); submarine must break through ice; visual methods are of negligible value; (4) in shallow water; submarine must transit under ice at a depth less than maximum draft of the ice canopy and must vertically dive in bottom–limited waters; (5) near icebergs; submarine must detect at maximum speed isolated ice masses extending below operating depth; and (6) in channels, island passages under an ice canopy possibly containing icebergs.

Inertial navigation equipment backed up by conventional gyrocompasses is now routinely used on submarines to navigate throughout the Arctic Ocean. A celestial fix is taken periodically to check the position given by inertial navigation. Electronic navigational aids are not yet established for coverage of the Arctic Ocean.

Under–ice piloting is done almost exclusively by the use of sonar in correlation with local knowledge of the bathymetry and ice conditions of the operating area. The sonar system is diagrammatically shown in FIGURE 1. A forward–looking sonar beam, narrow in vertical angle, is used to detect ice projecting down to ship's cruising depth: for example, icebergs or deep pressure ridges. Experience on U.S.S. *Seadragon* in cruising through Davis Strait and Baffin Bay has shown that sonar can be used successfully to pilot the submarine at full speed through a zone containing many icebergs. Where there is sufficiently deep water, for example, the central Arctic Ocean, cruising depth is set sufficiently deep to clear all pressure ridges easily, or the very rare ice island, draft perhaps 160 feet. However, in shallow areas, for instance the Bering, Chukchi, and east Siberian seas, or other approaches on the continental shelf, the presence of pressure ridges greatly influences the operations, requiring careful piloting and accurate, detailed knowledge of the bathymetry and sound transmission conditions of the area in transit. The forward–looking beam is used to pilot the submarine past ice ridges that extend too deeply. The downward–beamed ship's echosounder gives

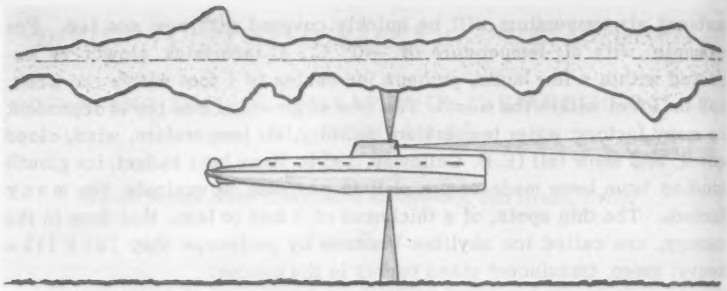

FIGURE 1. Sonar system for cruising under sea ice.

clearance above sea bottom. Ship's speed must be set in accord with distribution of heavy ridges and water depth.

The very broad, flat underwater plateau that forms the Bering and Chukchi seas and Pacific entrance to the Arctic Ocean, has a water depth of 125 to 180 feet and is more than 900 miles in extent. During winter, the ice canopy over this great shallow area contains numerous newly formed pressure ridges as well as old ridges from the permanent arctic pack. The U.S.S. *Sargo* transited the entire area during February 1960 in both north and south directions in order to investigate the winter ice canopy and experiment with ice piloting by sonar in shallow water. The expedition was designed to present the most difficult under–ice passage envisaged in arctic regions, and to examine critically the adequacy of under–ice sonars.

Specific bathymetric features of the shallow areas, for example, sea valleys, or even a slightest depression, have special significance to submarines operating under an ice canopy. These features give increased sea room that is all important and can be used to determine position or guide the approach to the coast. The Barrow sea valley, which lies off Point Barrow and has been described by Fisher *et al* (1958), is such a feature. It was used by submarines *Nautilus* and *Seadragon* both to enter and to leave deep water under the summer ice canopy of the Arctic Ocean.

An upward–looking sonar (FIGURE 1) records a continuous profile of the undersurface of the ice canopy, which gives a precise measurement of draft. The polynya (summer), or ice skylite (winter), suitable for the submarine to surface in, is chosen from this profile record as the submarine passes underneath the canopy. If a particular spot is chosen in which to surface, a turn is made to bring the vessel back and to hover directly under the chosen spot. By ballast control, a vertical ascent is made into the chosen polynya, or ice skylite. The ascent is guided by a vertical sonar screen and upward–scanning sonar, illustrated in FIGURE 2. The scanning sonar delineates the boundary of the skylite, and the upward screen of six fixed beams determines the ice draft above the entire length and beam of the vessel. The submarine must pass almost directly

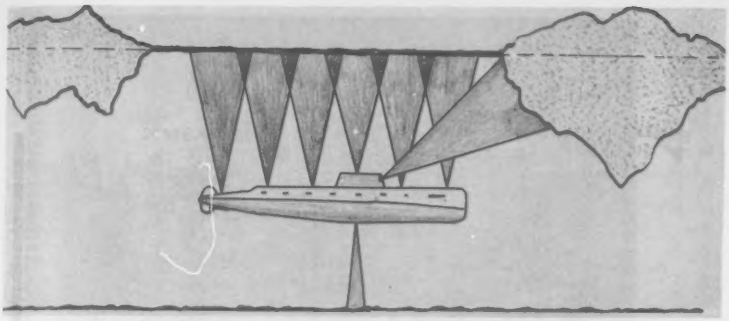

FIGURE 2. Sonar system for surfacing in ice.

under the polynya, or skylite, in order to recognize a suitable region for surfacing; hence surfacing depends on sufficiently high frequency and random distribution of suitable polynya, and/or skylites.

An ice profile record is shown in FIGURE 3, taken in the marginal sea–ice zone by diesel–battery submarine moving at a 3–knot speed. The vertical scale (B) gives the distance in feet from the submarine's deck, where the echosounder was mounted, to open water or ice overhead. The intense echo from the highly reflective, open–water–air interface gives a strong, sharply defined trace easily identified though the open water may cover only a small part of the total solid angle insonified by the echosounder. Surface waves observed near the edge of the ice zone are clearly shown. The ice draft is obtained by measuring the depth the ice trace extends beneath the open–water trace. As shown by J. H. Brown and E. E. Howick (1958), sea ice contains many minute air bubbles 0.1–mm. diameter in order of magnitude that are intense sound scatterers and give sea ice the acoustical characteristic of volume scattering very similar to that of a surface ship's wake, (Lyon, 1948).

In further illustration, the variable form of individual sound pulses scattered back from sea ice is shown in FIGURE 4. An oscillogram of the sound pulse (frequency 22 kc.) reflected back by the open–water surface is shown by example 1 (FIGURE 4), and shows the fairly steep front of the pulse and the trailing tail due to the effective breadth of the sound beam. The horizontal swing of the oscilloscope trace represents amplitude of the echo, and the vertical time scale is given as depth in feet beneath the open water surface by arbitrarily setting zero at the apparent steep front of the open water echo pulse. Example 3 shows sound scattered back of nearly uniform intensity from throughout the whole underwater body of sea ice, apparently about 22 feet in draft. Example 2 shows open–water reflection and ice scattering, whereas example 4 appears to indicate the presence of a well-defined bubble layer, or air pocket near the bottom interface.

For high speed (15–knot) and 400–foot deep cruising under ice by

FIGURE 3. Echosounder record of ice canopy, marginal zone.

FIGURE 3. Echosounder record of ice canopy, marginal zone.

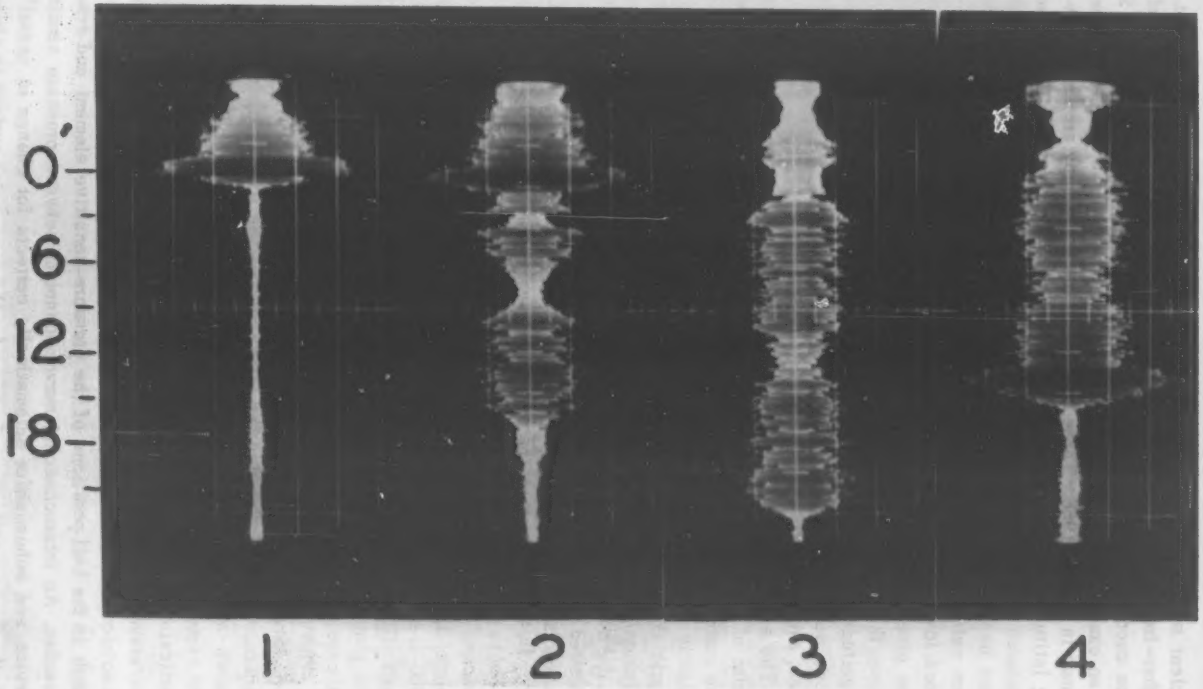

FIGURE 4. Sample oscillograms of reflected pulses from open water and sea ice.

nuclear submarines, it was necessary to use a much sharper–beamed, higher–frequency (150 kc.) echosounder to profile the ice canopy than had been used on the early work with diesel–battery submarines. FIGURE 5 is an example of the profile trace obtained during the *Nautilus* polar transit in August 1958. Three samples of the ice canopy are shown, giving latitude and longitude of each. Horizontal and vertical scales are measured in feet. Ice draft is again determined by measurement of the trace beneath the occasional trace spots of open water. However, the open water trace is more difficult to recognize than on the former, low–speed, low–frequency profile records. At higher frequency, bubble layers also give intense, sharply defined reflections. In addition, the record shows the variation in submarine's cruising depth, 3 feet, in order of magnitude; for example, note the wavy trace of a 1000–foot open polynya shown near the right side of the sample taken at 88° N. latitude (middle trace, FIGURE 5).

The samples distinctly show the progressive, general change in character of ice canopy from Pacific to Atlantic side of the Arctic Ocean. The number of pressure ridges per unit distance is much greater on the Atlantic side. Obviously these profile records can be used to obtain synoptic characteristics of the ice canopy, as illustrated by the two distribution graphs of FIGURE 6, which are results of the profile obtained on the *Nautilus* transpolar transit. The transit required 96 hours and followed a straight course along meridian 155° W–25° E. from Point Barrow across the pole to 86° N., then course changes to make 80° N., 00°. In the upper graph, the number of open water spaces per 10 nautical miles is plotted against latitude along the transit course. The number of spaces, 100 feet or greater in length, is given by the line–connected points; the number of spaces, 300 feet or greater by vertical lines, and 1000 feet or greater by vertical bars. In the lower graph, the average draft of the ice (in feet) is plotted per 10–mile increment of ice profile. The graph reflects the much higher density of pressure ridges on the Atlantic side of the transit.

Because observation of open water during winter is highly improbable, the convenient reference level for ice-draft measurement is lacking; particularly lacking during the very season when ice thickness must be known most accurately to accomplish surface breakthrough. Therefore the absolute hydrostatic pressure at the vessel is used to compute the vertical distance to the sea surface knowing the density of seawater and the gravitational constant. The pressure-measuring device must have an absolute precision of 0.1 per cent and correct for error due to roll and pitch in the hull positions of the pressure-sensitive element and echosounder. An interconnected servomechanism between pressure sensing device and echosounder automatically corrects for change in vessel's depth. Consequently the echo trace for the open-water surface is always set at the top zero line of the recording paper, and ice draft is read di-

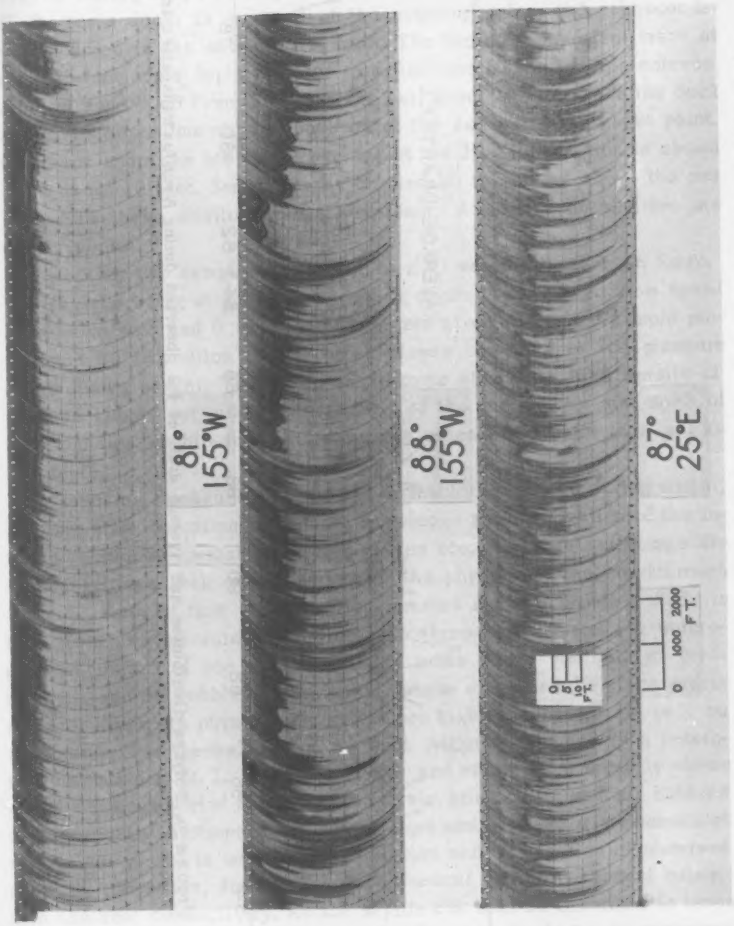

FIGURE 5. Sample echosounder records of ice canopy, *Nautilus* 1958 transpolar transit.

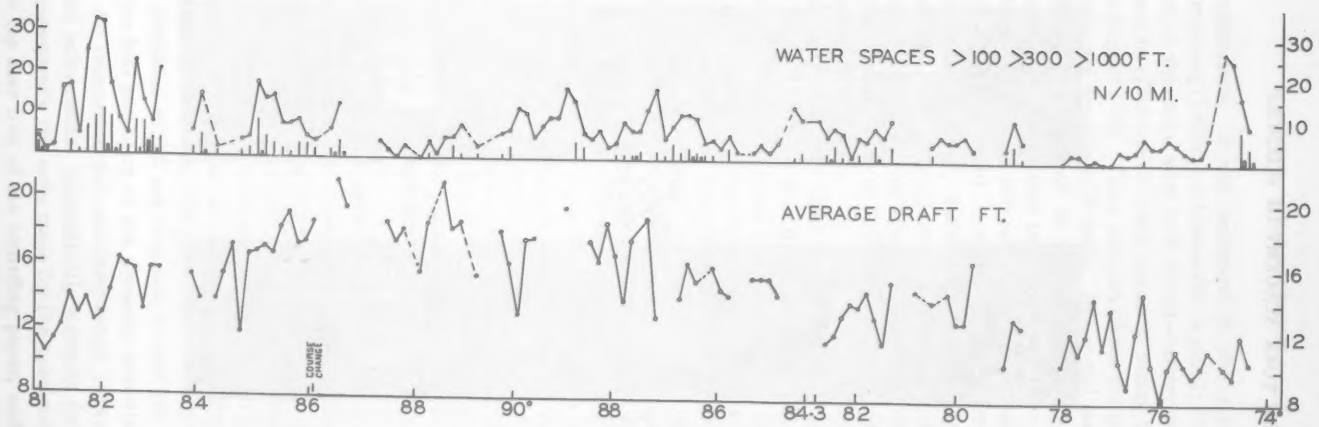

FIGURE 6. Polynya distribution and average draft of ice observed during *Nautilus* transpolar transit.

rectly as depth beneath the zero reference line. Sound frequency was further raised to give a sharp profile line of the undersurface, as illustrated in FIGURE 7. The horizontal scale is in nautical miles and the vertical scale in feet beneath open-water surface. Three sample traces are shown. The top trace was obtained on *Sargo* during transit of the shallow Bering Sea, February 1960. The dark, nearly level trace at about 95 ft. scale depth is a record of the outgoing pulse; the echosounder was mounted in the submarine's deck. The broad, intermittent trace at about 75-foot scale depth was due to reflections from a trailing antenna cable streaming aft from the top of the sail about 20 feet above the deck and gives approximately the position of the submarine's highest point. Clearance under the ice ridge recorded at the 2½-mile position is shown to be about 10 feet. *Sargo* usually cruised 20 to 35 feet above the sea bottom in these shallow water situations. A number of skylites are clearly shown.

The other two sample traces (FIGURE 7) were also taken on *Sargo*, both in deep water at a 400-foot cruising depth. A change to slow speed between miles 5 and 6 in the middle record gives a detailed sample profile and an indication of the steep slopes observed in ice pressure ridges during winter. The third sample trace shows the high density of pressure ridges per mile characteristic of the ice canopy just north of the Canadian Archipelago; a few ridges extend to greater than a 100-foot depth.

In breaking through an ice skylite to reach the surface during winter, the submarine operation implicates knowledge and observation of the intrinsic physicochemical properties of sea ice. Although surfacings are successful, we lack understanding of the physics of the breakthrough process. Gain of this understanding remains a major problem study in both field and laboratory. Sea ice is a three-phase system, a heterogeneous mixture of ice crystals, liquid brine cells, precipitated cryohydrates, and air bubbles. Continuously phase changes take place within sea ice; hence its physical properties are highly dependent not only on temperature but thermal history as well. Although sea ice is a heterogeneous mixture, D. L. Anderson (1960) and others have recently shown that the arrangement of ice and salt crystals, brine cells, and air bubbles is sufficiently systematic to permit representation by a mathematical model. The model is useful for description and explanation of observed physical properties, for example, mechanical strength, thermal expansion and heat conductivity. An ice skylite can then be described in terms of infinite plate theory if an appropriate function is chosen to represent strength in terms of thermal history and temperature gradient in the plate.

The uppermost layers are of near-ambient air temperature (perhaps -40° C., only a very minute amount of salt, magnesium chloride, still in solution) and, therefore, have highest strength. The bottom face is at

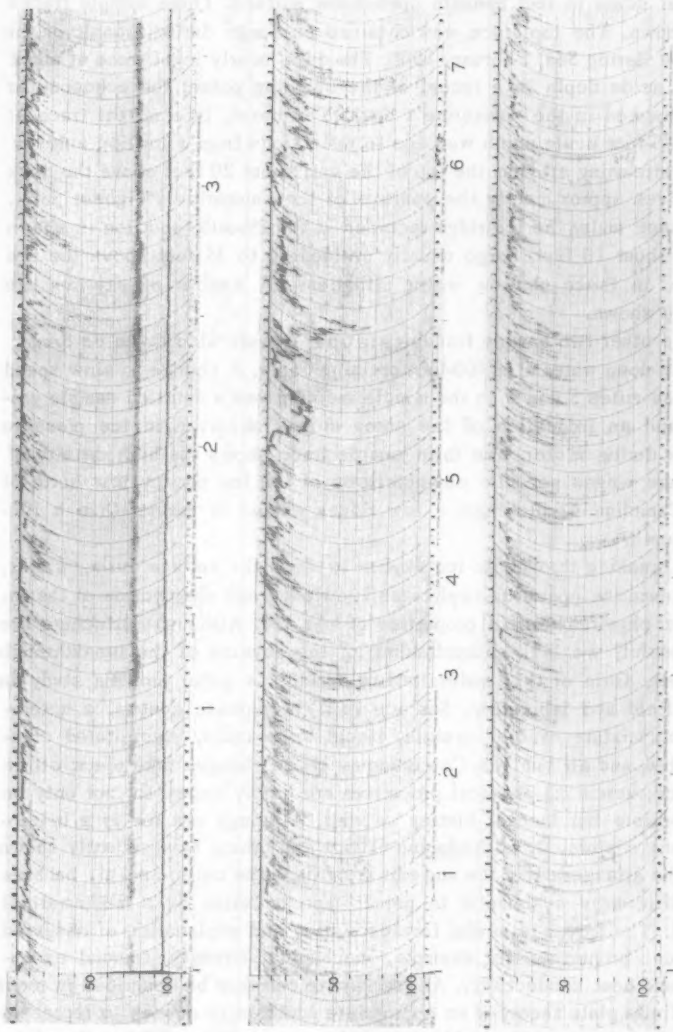

FIGURE 7. Examples of ice profile record obtained by hydrostatic servo-controlled echosounder (Sengo, 1960).

sea-water temperature and is a skeletal ice crystal structure of indefinable strength. At initial impact of the vertically moving submarine, the skeletal structure crushes and packs; it then imparts momentum to the top layers of the ice sheet until fiber stress rises above ice strength, and the sheet breaks. Neither the time-rate change of momentum nor integrated momentum impulse are known. The problem was further complicated when experience on the *Sargo* cruise indicated that many surfacings were through laminated sea-ice structures. The skylite had been formed by one uniform ice sheet (perhaps 6 inches thick) slipping on top of another similar sheet; the process again repeated to form a multiple layer structure, likely of strength characteristics quite different from that of undisturbed ice.

Successful operation of a submarine under sea ice has meant that many oceanographic parameters of the Arctic Ocean could be observed, in addition to profiles of the sea-ice canopy. For example, a precision depth recording is taken wherever the submarine goes, quickly and readily extending bathymetric information. Water temperature, salinity and transparency, amount of ambient light, earth's gravity, and plankton population are observed continuously or sampled periodically by instruments carried on or within the hull. The data have been or will be reported in papers published by the investigators for whom the data were collected or who are experts in the specific field to which the data apply.

The many submarine expeditions into the Arctic Ocean during the past 15 years have been carried out by the submarine forces of the United States Pacific and Atlantic Fleets. Skill, inventiveness, and willingness of officers and men to conduct undersea experiments have made the expeditions possible. The scientific work has been the cooperative effort of many scientists, laboratories, industries, universities, and institutions, both in the United States and Canada. It is impossible within the scope of this paper to recognize the significant contribution each individual has made. However, it is pertinent to this paper to note the work of A. H. Roshon and his group for development of under-ice scanning sonars and of L. L. Morse and W. E. Schatzberg in developing the ice-profiling echosounders.

Acknowledgment

I feel personally indebted to the late Harald Sverdrup for inspiration and guidance at the beginning of the under-ice experiments in 1946.

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FIGURE 7. Examples of ice profile record obtained by hydrostatic servo-controlled echosounder (*Sargo*,

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CEMENT AND CONCRETE TECHNOLOGY IN THE UNION OF SOVIET SOCIALIST REPUBLICS*

Ernst Gruenwald**
Lone Star Cement Corporation, New York, N. Y.

In becoming a highly industrialized economy, the Union of Soviet Socialist Republics has become widely urbanized, with 45 per cent of its people in cities and towns (many of which did not exist before World War II). The war greatly aggravated the already substandard conditions in the crowded prewar cities, for millions were made homeless and about 1,700 towns and 70,000 villages destroyed.

To meet the need for homes and factories, Soviet authorities have resorted to large-scale planning and a standardization of building designs and construction practices possible only in a totally controlled economy. Mass production and assembly line techniques have been applied to construction to speed output, save materials, and offset the rigorous winters.

Fifteen million new apartments are to be built for home-hungry Soviet citizens by 1965 under the present seven-year Plan. Little steel is available for construction, and concrete (largely precast) is preferred due to its extreme adaptability, simplicity, and low cost. Precast concrete accounted for about 40 per cent of the 1959 output of 59 million cu. yd. There are 2,000 precast plants, 60 of them in the Moscow region alone. Half of the planned 1965 output (105 million cu. yd.) will be precast, including 15 million cu. yd. of prestressed units. Five prototype plants have been designed for 26,000 to 240,000 cu. yd. annual output of precast concrete.

The Cement Industry

This vast program has required a fantastic expansion of cement production. The entire Soviet output from 1917 through 1940 (about 334 million bbl.) would serve only a year's needs in the United States at our present construction level. Since the war, the Soviet cement industry has mushroomed, producing 267 million bbl. in 1960, and is aiming for 475 million in 1965. To attain this goal they must add the equivalent of our Lehigh Valley District's cement-producing capacity (40 million bbl.) each year through 1965! Half the added production will come from new plants.

*This paper, illustrated with slides, was presented at a meeting of the Division on May 10, 1961.

**One of a party of United States concrete specialists that inspected the Soviet Union's construction industry in the summer of 1960, visiting five research and development centers, four cement plants, nine precast concrete plants, and construction sites in several large cities.

The Soviets produce five sacks of cement per capita compared to our eight. Housing takes 20 per cent of their output and industrial construction 58 per cent compared to our 21 per cent and 44 per cent respectively. Roads get only 6 per cent of Soviet cement against 25 per cent of ours. Dams and other large basic developments share most of the remaining Soviet output, while flood control, irrigation, and farm construction account for our balance.

Virtually all United States cement is portland, but only 46 per cent of the Soviet is true portland, portland slag accounting for 33 per cent and pozzolan for 18 per cent. Both the latter require less clinker-producing capacity than regular portland. Soviet specifications also permit the addition of up to 10 per cent inert material to cement, making it still more difficult to gauge clinker-producing capacity.

The planning, design, and erection of new cement plants is centralized in two institutes: one in Leningrad, the other in Kharkov. The Leningrad Institute, responsible for two thirds of the new plants has branches in Moscow and Novorossisk and a staff of 1,000. These institutes are available to existing plants for consultation and other services.

All aspects of cement plant design and operation, except geological investigation, fall within the scope of these institutes. Research is conducted in many aspects of cement production, and a pilot plant is operated. A special section studies foreign technical literature, translating all important papers.

Cement plant design has been standardized on four prototypes: one dry process plant and three wet process. About 85 per cent of the new capacity will be wet. The dry plant, for use where moisture in the raw material is under 10 per cent uses an ACL-type kiln 13' × 197' with sintering grate. The wet plant designs call for one kiln capacities of 10,500 bbl./day (with a 16½' × 607' kiln), 7,000 bbl./day (14'9" × 558' kiln) and 5,000 bbl./day (13' × 492' kiln).

The prototype plants are compact and have ample room for expansion. Most kilns will be fired by natural gas, large quantities of which are now available. Jaw crushers and hammermills will be used exclusively. All grinding will be done in 10½' × 49' mills. A plant in the 5 to 6 million bbl. category would require more than 2 years to build if given full priority for labor, materials, and equipment.

Some of the equipment and machinery will be imported; however, Soviet technology has advanced to the extent that a plant at Krasnodar now specializes in cement machinery.

My group visited cement plants in Belgorod, Sebriakov, Novorossisk, and Rostavi, all built in the 1950s. These tend to large capacities and larger machinery than are common in the United States and serve much wider markets. Raw materials are excellent, and methods and techniques are similar to our own. Operating equipment is well maintained,

but building and property maintenance and plant housekeeping leave much to be desired. Dust control is poor.

Storage at most plants is sufficient for only about two weeks' output. Virtually all cement moves in bulk via rail, much of it in open cars with considerable loss en route (10 per cent of the 1959 output was lost).

Safety receives little of the consideration given it in the United States. Such things as hand-rails, steps, and ladders are not built into the designs. Hard hats, safety shoes, or goggles are not worn. Each plant, however, had a well-equipped clinic or dispensary with full-time doctor or nurse.

Characteristic of all plants visited is a prodigal use of labor (a condition noted by individuals from the United States inspecting other Soviet industries). Despite considerable emphasis on mechanization and automation, the plants had three times as many workers as would be found in plants in the United States of similar size, and functions that we entrust to skilled employees they restrict to engineers. As many as 25 per cent of the workers were women.

Quality control at the cement plants visited seemed adequate, tests being similar to those used in this country.

Cement in the Soviet Union is manufactured to a grade system different from our method of specification. Grade is determined by the 28-day compressive strength of 7 cm. mortar cubes. Grades 300, 400, 500, and 600 are currently manufactured. Mortar cubes for testing are made with a stiff consistency and a w/c ratio of 2.7 to 3 gal. per sack of cement. United States tests use a plastic mortar with a water content of about 5½ gal. per sack. Direct comparisons are difficult due to difference in test methods; the Soviet tests tend to give 40 to 50 per cent higher compressive strengths than would be obtained if tested by our methods.

Some of the Soviet cement men recognize that present specifications and test methods are inadequate and do not always indicate the quality of the concrete made from the cement. They are considering some form of plastic mortar strength test using 40 × 40 × 160-mm. mortar bars for transverse tests plus compression tests on the broken halves. Sharp, angular silica sand is used instead of the carefully graded sands required elsewhere. A w/c ratio of 0.40 is under consideration (rather than the 0.50 common in Europe and the United States).

Many talented and capable people were found in the Soviet cement industry. They were well informed of cement developments elsewhere in the world. Some contribute regularly to the foreign technical press, particularly the German. All were eager for "shop talk" and appeared to give straightforward answers to all questions.

Institutes in Leningrad, Moscow, and Kharkov are devoted to fundamental research into the chemistry of cements and silicates. All have large staffs of engineers and technicians. Impressive work is being done on clinker, cement chemistry, and refractories. Among the more

interesting basic work are X-ray analysis of silicates and the extraction of hydrosilicates. The engineers and technicians are very interested in infrared petrography. A special furnace for testing refractory concrete wherein heat and pressure are simultaneously applied was noted.

The Concrete Construction Industry

Three concrete prefabrication plants were visited in Moscow, two in Leningrad, and one each in Kiev, Kharkov, Sverdlovsk, and Stalingrad. These are large industrial enterprises covering as much as 19 acres. The main building, devoted to casting, is usually two to three bays wide (50 to 60 ft.) by 300 ft. long. Materials handling buildings and storage areas are well integrated. The investment for such factories runs 7 to 11 million dollars.

The plants were equipped with elaborate moving machinery for assembly-line production, well designed, and varied to suit the different types of units to be produced. These included cored floor slabs such as Spancrete or oversized Flexicore, ribbed slabs, waffle slabs, solid slabs, and wall sections with windows and doors completely installed. Wall sections may be of lightweight concrete, sandwich waffle slabs, and ceramic-faced slabs.

One-story-high box units are a new development. A box section, complete with exterior and interior walls, floor, and ceiling, is manufactured as a unit, delivered to the site, and stacked upon others to form a building. Toilet and bath are cast as a unit and installed in prefabricated apartments.

Several housing developments were visited, some completed and some in construction. Floors are standardized at 19- and 23-foot spans, with a 9-foot story height. A typical project of 16 houses built of prefabricated panels covered about 29 acres, using about 20 per cent of the land for buildings. Population density is 250 persons per acre. The project provided 291,000 sq. ft. of living area in 1-, 2-, and 3-room apartments at rentals of 7 to 12 per cent of monthly wages. Apartments are small (averaging about 410 sq. ft.) but they do provide shelter.

The precast sections are transported on special trailers to jobsites by an agency that is separate from both the factory and erection organizations. There appears to be a shortage of erection crews, and many apartment buildings were half-finished, with the components stored at the site. Most erection is by hammerhead crane. For the box-type construction a special gantry will straddle the building, picking up the 6-ton units from their trailer and placing them in position.

Precast sections are normally connected by welding steel straps at the corners. The welding was not impressive, and the Soviet engineers recognize the danger of failures. Jointing is also a problem. Workmanship in general is poor, and maintenance will certainly be a problem. Buildings only a few years old appear to have been in use for years. Cracking and leakage were noted.

Soviet apartment-house architecture is generally uninspiring. However, it answers the basic need for adequate, withal cramped, quarters. All the new apartments have sanitary facilities and central heating: missing in the older houses.

Soviet concrete is rated in grades similar to their cements, ranging from grades 200 to 400 (2,850 to 5,700 psi), determined on cubes that test 15 to 20 per cent higher than our standard 6 × 12 inch cylinders.

Concrete aggregates are a serious problem. Some areas have no adequate sand of proper gradation. Coarse aggregates are not available in other areas. This has caused the Soviet Union to devote much attention to the manufacture of lightweight aggregate.

Soviet concrete uses a low w/c ratio to save cement, making a dry, harsh mix that requires great care for proper placement. Concrete surfaces are generally poor, and few precast members would be acceptable in this country just on the basis of appearance alone. Curing temperatures up to 200°F. were noted.

The methods used in concrete plants are known in this country, the major difference being the high degree of standardization that makes possible large-scale mass production. The practices in use are well adapted to the controlled economy, which permits them to operate in ways that would not be acceptable under free enterprise. Soviet plants are expensive to operate and maintain, and they tend to be overequipped. tend to be overequipped.

Plant management in the Soviet Union differs from our own. Managers appointed by the government are given rigid budgets and specific plans of operation against which performance is measured. The manager is responsible for output, but must function in cooperation with the union chairman elected by the workers. Together they work out collective labor contracts, with wage scales subject to state approval. The union chairman is also responsible for settling labor disputes and for improving working and living conditions.

Workers are hired off the street or through contract with the union. There is a six-day probationary period. Firing must be approved by the union, and a worker can quit or change jobs only if he gives twelve days' notice.

Plant managers produce "profits" by operating below allocated budgets, by producing above the required volume, and by producing better quality products that net a higher price. These "profits" can be spent for plant improvements or (with the approval of the union chairman) as incentive bonuses and to improve working conditions.

As with cement men, Soviet concrete and construction men are keenly aware of quality problems. Expediency remains the rule, however, until they begin to catch up with the tremendous need for concrete structures.

Signs Noted in Soviet Cement Plants by E. Gruenwald

"Our task is to learn the enterprise of Communist labor."

"Remember each time we must reline kilns it costs us 85,000 rubles." (under kilns).

"Carry on the struggle for saving equipment and eliminating waste."

"The Plan is the Law." (That is, the Seven-Year Plan)

"Let us fulfill the decisions of the 21st Congress."

"Glory to the Communist Party and the Soviet Union."

"The nuts, bolts, small tools that cost a few kopecs eat up the rubles. Take care of the small expenses and the kopecs will take care of the rubles."

"Think, act, and work like a Communist."

"Save electricity, it's the blood of industry."

"Worker, remember, your work is the best contribution toward peace."

"This shop is struggling to win the honor of being a Communist shop."

"A clean place is a healthy and happy place to work."

"We will give the country more cement."

(The repeated reference to "Communist" is interesting. The Communist Party is the only political party permitted in the Soviet Union. Its membership is less than 4.2 per cent of the total population.)

SECTION OF PHYSICAL SCIENCES

RECENT DEVELOPMENTS IN THE FIELD OF ATOMIC COLLISIONS*

Arnold Russek

Physics Department, The University of Connecticut, Storrs, Conn.

The subject matter of this paper is divided into two distinct parts. The first deals with the considerable amount of information concerning the structure of atoms and molecules that can be learned from scattering experiments. The second part is concerned with high-energy atomic collisions, the particular field being studied theoretically and experimentally at the University of Connecticut.

A convenient means of classifying experiments in atomic collisions is by the energy of the bombarding projectile. Thus we speak of low-, intermediate- and high-energy atomic collisions. The low-energy range (bombarding energies of a few electron volts or less) yields valuable information on molecular binding, chemical kinetics, and the kinetic theory of gases. At higher energies (a few electron volts up to a thousand) much can be learned about some of the processes that go on in a highly heated plasma, yielding data of great importance to those attempting thermonuclear power and to those attempting to understand the physics of the sun. At even higher energies (between one thousand and, perhaps, one-half million electron volts), information can be obtained pertaining to the damage produced in solids by fission fragments and radiation and, perhaps, also about the collapsed state of matter that occurs in the white dwarfs. At still higher energies (above one million electron volts) the binding energies of electrons to a nucleus are negligible compared to the bombarding energy, and their presence or absence may be neglected. In this latter range, nuclear reactions begin to occur, and such collisions therefore belong to the domain of nuclear physics. In this regard, it should be parenthetically mentioned that in the energy ranges that have been classified under atomic collisions, the nuclei of the colliding atoms never get close enough to each other for any nuclear effects to take place.

Of fundamental importance in any scattering experiment is a quantity called the differential cross section. It is the effective differential area presented by each target for the particular scattering process (for example, elastic scattering, scattering accompanied by electron exchange or excitation of one or both atoms) in which the projectile is deflected

* This paper was presented at a meeting of the Section on May 17, 1961.

The Division of Psychology held a meeting on May 15, 1961, at which Jerome M. Goldsmith, Alfred B. Amler, Samuel Rosmarin, of the Hawthorne Cedar Knolls School, Hawthorne, N. Y., and Grace M. Abbate of the New York Mental Health Board, New York, N. Y. presented papers on "The Interprofessional Treatment of the Disturbed and Delinquent Adolescent." No manuscripts have been received.

(scattered) by an angle between θ and $\theta + \Delta\theta$. Denoted by $\sigma(\theta)$, the differential scattering cross section is defined as the number of projectiles scattered per unit solid angle per unit time per target particle in the direction making an angle θ with the direction of the incident beam, for unit intensity projectile beam. In order that a measurement of this quantity be significant, the density of targets must be of sufficiently small size to make the probability of any projectile making multiple collisions negligible. The total cross section is the integral of the differential cross section over all possible directions of scattering and is the total effective area presented by the target for the process under consideration.

The differential or total cross section for some process is the end experimental result of any scattering experiment. It is at this juncture that theory and experiment are compared. A theory or model of the process under consideration predicts the cross section and thereby stands or falls as it is confirmed or contradicted by experiment. From the experimental cross section data for atomic collisions, the theoretician can work back and find the forces and potentials between colliding atoms. Finally, in many instances in kinetic theory, just the experimental cross-section results themselves are needed to be inserted as empirical parameters in the kinetic theoretical approach to some process such as diffusion or chemical reaction rates. Let us now consider in detail the general experimental setup and what can be learned from scattering experiments in the three energy ranges.

The Low-Energy Range

A low-energy beam of atoms or molecules is obtained from an oven with a small hole in it from which a stream of the atoms or molecules issues in all directions. This is made into a beam by a pair of collimating slits or holes. Moreover, if a monoenergetic beam is required instead of the Maxwell-Boltzmann distribution characteristic of any thermal source, this is accomplished by a "time of flight" velocity selector. The collimated beam is blocked by a shutter that periodically opens for a short time to let a burst of atoms through. Downstream or, rather, down-beam, a second shutter opens for the same length of time at a precisely timed interval later, so that only atoms moving with velocity $v = D/T$ will be able to pass through both shutters (D being the distance between shutters and T the time interval between the openings of the two shutters.) The shutters are usually holes in rotating disks. With such a setup, it is possible to get a monoenergetic beam of atoms, even of atoms that do not ordinarily exist singly in nature, such as lithium, cesium, and atomic hydrogen. If neither projectile nor target exists in the required state (for example, the scattering of mercury by potassium), a crossed-beam experiment must be performed, that is, two beams are formed at right angles to each other.

Experiments involving the scattering of suitably chosen beams by suitable chosen targets can probe the forces that exist between the atoms of the species used as projectile and target. This is illustrated in FIGURE 1. At low energies principally the long range attractive part of the interatomic force is probed, inasmuch as the energy of the projectile is not great enough to penetrate deeply into the repulsive core. For example, Pauly's group[1] at Bonn University, Bonn, Germany, has reported confirming the theoretically predicted C/r^6 van der Waals attractive potential for potassium scattered in nitrogen. At higher energies (including the intermediate and high-energy ranges) the repulsive part of the interatomic potential can be explored.[2] The results obtained from such experiments furnish data important to the kinetic theory of gases as well as molecular structure.

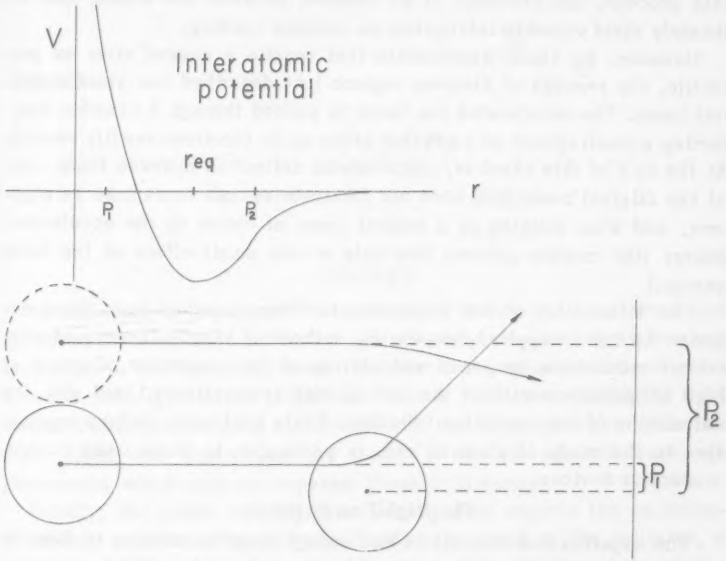

FIGURE 1

Another important aspect of the low-energy collision work is that of chemical kinetics. To date, most of our knowledge concerning this mechanism has come from measurements of chemical reaction rates as functions of temperature and concentration. Although a great deal has been learned in this way, the finer details are obscured by lack of independent control over the reacting species and their energies. This control can be had by the atomic beam collision experiment.[3] Along these lines Taylor and Datz[4] have used crossed beam techniques to measure

the cross-section and threshold energy (that is, the activation energy) for the gas phase reaction $K + HBr \rightarrow KBr + H$.

The Intermediate-Energy Range

In this energy range the projectile beam cannot be obtained by thermal means, and is obtained instead by electrostatic acceleration. This requires that the projectile atoms be ionized, and these are usually obtained from a gas discharge. The fact that the projectiles are ions instead of neutral atoms does not constitute too much of a drawback. As a matter of fact, some of the more important experiments in this energy and the high-energy ranges concern themselves with the cross section for a process known as electron capture,[5] that is, the capture of an electron from a neutral atom by an ion whizzing by. A thorough knowledge of this process, the exchange of an electron between two atoms, can ultimately yield valuable information on valence bonding.

However, for those experiments that require a neutral atom as projectile, the process of electron capture just described can yield a neutral beam. The accelerated ion beam is passed through a chamber containing a small amount of a gas that gives up its electrons readily enough. At the exit of this chamber, electrostatic deflection removes those ions of the original beam that were not fortunate enough to capture an electron, and what remains is a neutral beam of atoms at the accelerator energy (the capture process has only a very small effect on the beam energy.)

The information of the intermolecular force obtained from these experiments can be applied directly, by methods of kinetic theory and statistical mechanics, to permit calculation of the properties of gases at high temperatures without the use of high temperatures,[6] and also the calculation of ion mobilities.[7] Studies of this kind have obvious application to the study of plasmas and, in particular, to those used in thermonuclear devices.

The High-Energy Range

The experimental methods in this energy range are similar to those in the intermediate-energy range. At these energies, the collisions are so violent that the outer shells of the colliding atoms are not able to stand up under the impact, and the atoms deeply interpenetrate each other,[8] producing multiple ionization.[9] Studies such as this can yield information on the range of, and damage produced by, nuclear-fission fragments. Moreover, collision experiments in this energy range provide the only terrestrial means of obtaining information that might shed light on the behavior of matter subjected to the extremes of temperature and pressure that occur in stellar material and, indeed, they may enable us to determine the precise conditions that lead to the ultimate collapse of matter as found in the white dwarfs.

The investigation in atomic collisions at the University of Connecticut has been exclusively in the high-energy range, and has largely been concerned with multiple ionization produced by hard scattering (that is, large angle collisions) in this energy range. FIGURE 2 shows a schematic of the experimental arrangement, and FIGURE 3 shows a sample of the data obtained for singly ionized argon atoms incident as projectiles on neutral argon.

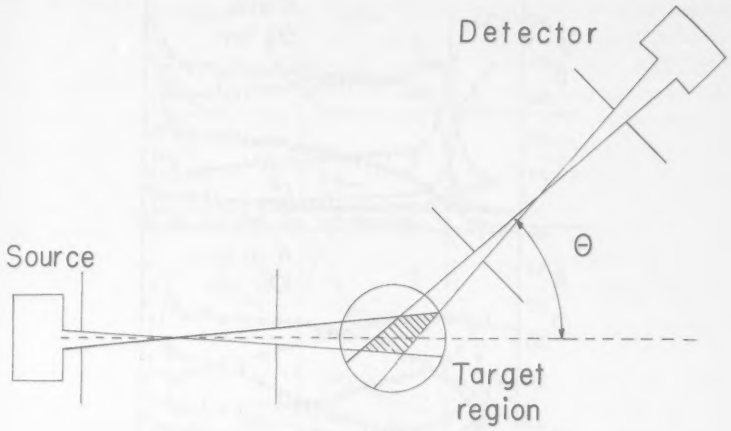

FIGURE 2

In three previous papers[10-12] a statistical theory has been developed to account for multiple ionization phenomena accompanying high energy atom-atom or ion-atom collisions. The first two papers treated collisions between noble gas atoms (eight electrons in the outer shell). The third treated collisions between atoms with from two to seven electrons in the outer shell and generalized the theory to include electron exchange phenomena, which also accompanies these collisions.

Briefly, the model developed in three papers regards the collision-ionization as a two-step process. First, as a result of the collision, a relatively small amount of the kinetic energy of translation of the atoms, E_T, is transferred to their internal degrees of freedom. Second, upon separation the "heated" atoms get rid of this excess energy partly by photon emission and partly by electron evaporation. The electron evaporation aspect of the model is based on four assumptions: (1) the energy transferred to the internal degrees of freedom, E_T, is distributed among the outer electrons only; (2) the energy transferred is statistically distributed among these electrons; (3) all of the energy cells have equal statistical weight; and (4) a uniform ionization energy is assumed. Any of the outer electrons that acquire more than this energy will escape regardless of how many others also escape. FIGURE 4 shows the computed

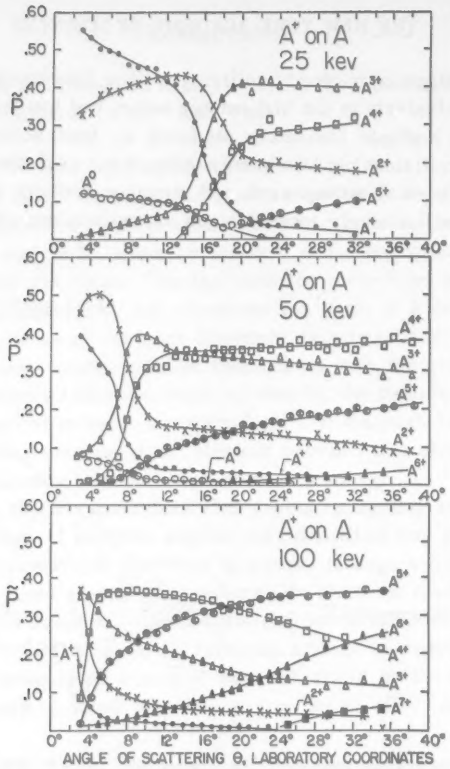

FIGURE 3. The experimental data for the ionization probabilities, $\tilde{P}_n$, for the case of singly ionized argon atoms on neutral argon atoms as functions of the collision parameters, angle of scattering and incident ion energy. Reproduced from Russek and Thomas[10] by permission of *Physical Review*.

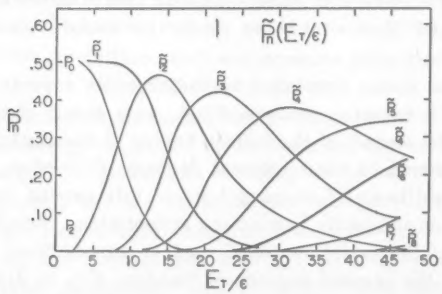

FIGURE 4. The calculated ionization probabilities, $\tilde{P}_n$, for the case of a singly ionized noble gas atom incident on a neutral noble gas atom plotted as functions of the energy E_T transferred to the internal degrees of freedom. The unit ϵ is one quarter of the ionization energy. Reproduced from Russek and Thomas[10] by permission of *Physical Review*.

ionization curves of the evaporation theory for a noble gas ion incident on a noble gas atom, and FIGURE 5 shows the comparison of the theory with experiment for Ar+ on Ar using empirically determined values for E_T as a function of the collision parameters.

Assumption 4 was somewhat unexpected and was incorporated into the theory only because it was absolutely required to achieve agreement with the data. Subsequent investigation into the nature of ionization

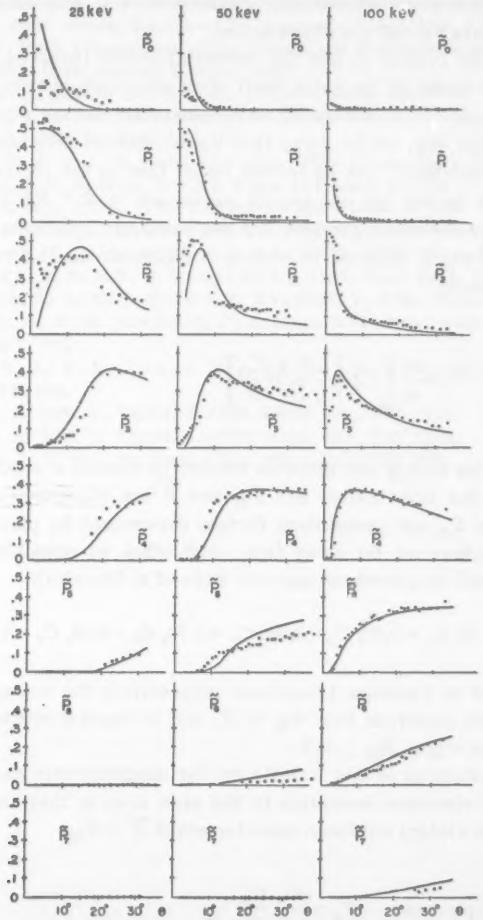

FIGURE 5. Comparison of the theoretical curves of FIGURE 4 with the experimental points of FIGURE 3 when the energy E_T as a function of the collision parameters is empirically determined. Reproduced from Russek and Thomas[10] by permission of *Physical Review*.

accompanying violent atomic collisions indicates, however, that it is radically different from the nature of ionization encountered in spectroscopic studies and, furthermore, that assumption 4 is to be expected on *a priori* grounds. The essential point that must be realized is that in spectroscopic studies multiple ionization is achieved by removing only one electron at a time, the remaining electrons always staying in unexcited states at the time. In atomic collisions, on the other hand, the entire ionization takes place essentially instantaneously, and even the electrons that remain behind are also excited.

In order more clearly to see the essential points involved, we take a brutally crude model of the outer shell of an atom (let us take argon as a specific example) in which the outer electrons are sitting statically on a sphere of radius R_M, as far away from each other as they can get, subject to this constraint. Let us further insist that in the ionization those electrons that do not get out are all moved out to $\overline{R} > R_M$ ($\overline{R}$ will be a function of the inelastic energy). On the basis of this crude model, the energy *per* electron required to remove n electrons can be computed by freshman physics.

$$W_n = \frac{e^2}{a_o}\left[C_8\left(\frac{1}{R_M} - \frac{1}{\overline{R}}\right) + \frac{C_n}{\overline{R}}\right] \tag{1}$$

Here, W_n is the energy per electron needed to remove n electrons to infinity, a_o is the Bohr radius and R_M and $\overline{R}$ are expressed in terms of this unit. The C_n are geometrical factors determined by placing n electrons on a sphere as far away from each other as possible (thus two electrons would be placed on opposite ends of a diameter):

$$C_1 = 1,\ C_2 = 1.75,\ C_3 = 2.42,\ C_4 = 3.08,\ C_5 = 3.70,\ C_6 = 4.34,\ C_7 = 4.90,\ C_8 = 5.53$$

The two terms in Equation 1 represent respectively the energy needed to move all eight electrons from R_M to $\overline{R}$, and to move n electrons from $\overline{R}$ to infinity; for argon, $R_M \simeq 1.3$.

The two extremes of this formula are the spectroscopic case for which $\overline{R} = R_M$ (the electrons remaining in the atom stay in their unexcited orbits), and the violent collision case for which $\overline{R} \gg R_M$.

Spectroscopic case: $$W_n = \frac{e^2}{a_o} \cdot \frac{C_n}{R_M} \tag{2}$$

Violent collision case: $$W_n = \frac{e^2}{a_o} \cdot \frac{C_8}{R_M} \tag{3}$$

It is seen from Equation 3 that in the violent collision extreme the energy per electron for removal is independent of the number of electrons removed. This ionization energy is approximately 100 ev.

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DIVISION OF ANTHROPOLOGY

NEW ANTHROPOLOGICAL DISCOVERIES AT SHANIDAR, NORTHERN IRAQ*

Ralph S. Solecki
Department of Anthropology, Columbia University, New York, N. Y.

The findings of the Fourth Shanidar Expedition of 1960 extended the cultural heritage of Iraq; it also contributed toward our knowledge of prehistory in the Near East. These contributions include the discovery of three new early man skeletons (Shanidar IV, V, VI), the additional remains of Shanidar II and III, which were discovered last season (1956-1957); a cemetery of 26 burials in the Proto-Neolithic layer of the cave; new data regarding the early domestication of animals and other faunal data; and data regarding climatic changes as reflected in fossil pollen and trace element analysis.

The two sites investigated, Shanidar Cave and the nearby open village site of Zawi Chemi Shanidar, are situated about 250 airline miles north of Baghdad in the Zagros Mountains. Shanidar Valley has been the scene of archaeological investigations since 1951 (Solecki, 1959). The staff of the fourth expedition included my wife, Rose L. Solecki, Jacques Bordaz, and myself, all of Columbia University; T. Dale Stewart of the Smithsonian Institution; and Dexter Perkins, Jr. of the Philadelphia Academy of Sciences, Philadelphia. Ibrahim el Zayri was the expedition's very able representative from the Directorate General of Antiquities of Iraq.

Jacques Bordaz, Rose Solecki, and I arrived in Baghdad June 1st. Dale Stewart arrived June 3. After all the necessary arrangements were made, excavation began at the village site June 20, and at the cave on the following day. A total of 11 weeks was spent in the excavation up to September 4, the close of work. Approximately 47 men were employed in the excavations.

Stewart, our physical anthropologist, remained in Baghdad from the time of his arrival until July 16, working over the Neanderthal remains found last season (1957). He spent between July 18 and August 15 with the expedition at Shanidar. Perkins, our paleo-zoologist, joined the field group on July 23, after some delay in arriving. He stayed at Shanidar to the end of the season. Both Perkins and Stewart profited greatly from

*This paper, illustrated with slides, was presented at a meeting of the Division on May 22, 1961.

The Fourth Shanidar Expedition reported in this paper was co-sponsored by Columbia University and The Smithsonian Institution, Washington, D. C. under a research grant from the National Science Foundation, also in Washington, D. C. The expedition received welcome cooperation from the Iraq Directorate General of Antiquities, Baghdad, Iraq, as in previous seasons, and the Iraq Petroleum Company, as in the past season, lent material assistance to the expedition.

the field experience gained in their specialties. It gave them a chance to observe the environment of Shanidar valley, and the field conditions under which the remains they were interested in were found.

Résumé of the Previous Seasons at Shanidar

During the previous seasons, 1951, 1953, 1956-1957, a very deep (nearly 14 m.) series of cultural deposits were found and outlined at Shanidar Cave. From top to bottom the sequence includes layer A, the recent to Neolithic horizon; layer B, divided into two parts, an upper Proto-Neolithic horizon (B1), and a Epi-Paleolithic or lower Mesolithic horizon (B2); layer C, the Baradostian horizon of Upper Paleolithic age; and the lowest stratum, layer D, the Mousterian layer of Middle Paleolithic age.

The village site of Zawi Chemi Shanidar, first excavated in the 1956-1957 season, is about 2½ miles from the cave. There are two distinct layers at the village site, including layer A, with ceramic remains dating between 600 and 1200 A.D. at the top, and a basal stratum, layer B, containing material of preceramic or what we call Proto-Neolithic age. It is the latter layer with which this report is concemed. It appears to be contemporary with the Shanidar Cave layer B1.

Descriptions of the Excavations

Zawi Chemi Shanidar: this village site excavation was extended to the north of the 1956-1957 work in an area measuring 112 sq. m., or 8 x 14 m. The depth, not uniform throughout, reached sterile soil at slightly more than 2 m. in the northern part of the cut. We gained an impression that the village site continued to extend in area and depth to the north, and grew increasingly complex. The excavation was left open for a future season. Several large pits were discovered at the base of the Zawi Chemi B layer. The purpose of these pits is not yet positively known; they may have been dug for the disposal of refuse, although it is more likely that they had originally served another purpose. The pits were crammed full of mammal bones, and ashes and charcoal from hearths.

Rose Solecki, who is in charge of the Zawi Chemi Shanidar project, is preparing a report on the work, detailing the finds made there. Notable among the 1960 season finds was a curved bone haft, probably a sickle handle, with a linear groove running the length of the concave side. Similar finds were reportedly made by the Danish expedition under Harald Ingholt (1957) of Yale University, New Haven, Conn., at Tell Shimshara in the Dokan district of northeastern Iraq. Flint blades were presumably set in the groove and held on place with an adhesive. A flint blade thus set in a bone haft was found in the comparable layer at the cave (see below). This artifact indicates that some kinds of grasses

were presumably cut by these early villagers of Shanidar valley; whether for winter feed for captive livestock, for the cutting of cereal grains, or other reasons is not known at present. Linking this specimen with an economy new to Shanidar valley reinforces other observations and factual evidence indicating a departure from the purely hunting and gathering subsistence in the area.

Shanidar Cave

We resumed the work discontinued at the cave in the 1956-1957 season. On the last day of the 1960 season, the excavation proper measured 12 m. wide (E-W) by 26 m. long (N-S), with two small appendage excavations, extending the maximum width to 16 m., and the maximum length to 34 m. The excavation was stepped down in depth. The appendages mentioned include a 4 x 4 m. pit in the east wall in the find area of Shanidar Neanderthals I and III, and a 2 x 8 m. extension at the northern end of the excavation. This latter exploratory cut was directed toward reaching the rear wall of the cave as planned, but in this we were disappointed. A cavern extension that had been hidden by the deposits of layer A was uncovered off the northeastern quarter, indicating that the rear of the cave lies considerably farther than had been thought in this area. The new cavern is a low ceilinged ovate cavity about 4 feet high and 125 feet long (N-S) by 40 feet wide (E-W). The cave was full of stalagmites and stalactites. Some pottery fragments of modern type and bones of goats and cattle were identified on the very damp floor. Some of the floor was earthen. Perhaps a portion of this cave extension was inhabitable during prehistoric times.

To facilitate the removal of the postcranial skeleton of Shanidar II, which had been of necessity left in place in 1957, a preparatory shelf-like step was cut above Shanidar II, removing the loose material of layer A. Next, a deep incision was made straight downward through layers B and C into layer D to the skeletal remains. These were moved by Dale Stewart. At the same time, the cut in which Shanidar I was found was extended in depth, in order to make sure that all of the information had been obtained. As this cut progressed, it was found necessary to remove a small block of soil that had not been excavated at a depth lower and to the west of the Shanidar I find spot. In this soil was found Shanidar IV. While Stewart worked on exposing these remains, an exploratory cut in the find place of Shanidar III, a couple meters to the south, resulted in finding additional remains of the latter. In a preparatory excavation just to the south of Shanidar III, the remains of a fifth skeleton, Shanidar V, were encountered. No sooner was this skeleton found than Stewart, who by this time had several skeletons of early man surrounding him, discovered that just beneath Shanidar IV lay a sixth skeleton, Shanidar VI. A summarized description of these finds is given below.

One of the objectives of this season was to cut a trench toward the rear, or north end of the excavation, in order to reach the cave wall. Work did not progress very far, for in the Proto-Neolithic layer (layer B1) a cemetery of 26 burials was found, bringing the total for all seasons of these remains from this layer to 28. Unfortunately the closeness of the end of the season did not permit completion of exploration in the area of this highly interesting discovery.

No new data were found in the Baradostian horizon (layer C), other than that derived from the nonartifactual studies summarized below. It appears that this is the only layer in Shanidar Cave that has not yet produced skeletal remains. In fact, we have no good skeletal knowledge of any Upper Paleolithic people east of the Levant.

Layer B of Shanidar Cave is now divided into two parts, based upon a faint though distinct stratigraphical difference in the soils, artifactual differences, and carbon-14 dating. There also appears to be a distinct climatic difference also, as indicated by fossil pollen and trace element studies. The lower portion of layer B has been designated as B2, with an industry rather like that of Zarzi (Garrod, 1930). Zarzi is late Upper Paleolithic, or Epi-Paleolithic or even Mesolithic in typology. None of these terms is expressly satisfactory for proper distinctions, and a type site name may be better used, as Zarzian. At Shanidar no new artifactual data was found in the Shanidar B2 layer, principally because we had barely cut into this horizon. It has been dated as 12,000 years B. P. (before the present), according to carbon-14 dating.

In the Shanidar B1 layer, lying above B2, a wealth of data was recovered this season. This layer is carbon-14 dated at about 10,600 years B.P. It is for our considerations coeval with the basal stratum, layer B, of the Zawi Chemi Shanidar village site, dated by the same method at 10,870 years B.P. The cultural contents of both comparative layers is quite similar. It appears likely that the cave was occupied during the colder winter months, while the village site was favored during the summer months. A similar tradition of wintering in caves and summering out in the open is followed by some of the Kurdish mountain people today. There is good evidence suggesting that between 11,000 and 10,600 years ago the Shanidar mountaineers had possession of an economy that had released them from a dependence upon a less flexible hunting-gathering economy. Several pits noted in the Shanidar B2 level (R.S. Solecki, 1955: FIGURE 6) may have been food storage pits, a feature known for a certainty in later more culturally and economically advanced horizons. However, at Shanidar Cave, there is no evidence that the people who had left the occupational horizon of Shanidar B2 had any knowledge of grinding or of pounding food with stones.

In the Shanidar B1 layer, within the northern extension area, was found the cemetery mentioned above, containing 26 burials, chiefly of

children and infants, lying at a depth of about 1 m. Several small platforms of rough stones were found. One of these was associated with a rough stone arc reminiscent of the stone enclosure found at the village site in 1957. On the small pavement of stones within the cave arc were found the partial remains of a skeleton. Grave goods were found with several burials. A few of the infant burials were literally burdened with thousands of well made beads of stone. Several expertly fashioned bone implements were found with the adult burials. One of the latter implements was a large bone dagger perforated for suspension at the basal end. A very singular specimen was a bone that looks as though it were made, like the others, from the broad rib of an animal, with a flint blade inserted in a side slit, and fixed in place with a lump of bitumen. This is the first specimen of its kind from Shanidar, and certainly the earliest dated in Iraq. There is clear-cut evidence that these people had ranged, or at least traded, quite far. The closest source for bitumen seems to be in the region of Kirkuk, about 100 miles to the south. This is a vastly different environment than our mountains. On the other hand, obsidian, which is found in the form of chipped artifacts in this layer, occurs in the Lake Van region of Turkey, about 125 miles to the north. A small pendant of copper was also uncovered in the burial area. This is a new element whose significance is not yet determined. Moreover, it is not yet certain whether it was intrusive or not.

The skeletal remains from Shanidar B1 present us with a potentially good population study. J. Lawrence Angel, of the Jefferson Medical College, Philadelphia, Pa., has agreed to examine these remains. They represent the best series we have of this cultural horizon east of Palestine.

The discoveries of the Shanidar IV, V, and VI skeletons, all maiure individuals, are summarized below. Included is a résumé of the work done to find additional evidences of Shanidar II and III, which had been discovered in 1957. Because of the soil qualities, none of the bones was mineralized; all were found in a fair state of preservation.

One of the main objectives of the 1960 season was to uncover the postcranial skeleton of Shanidar II, lying at a depth of about 7.4 m. (Solecki, 1960: 620). It was possible to remove only the skull in 1957. When the remains were finally uncovered after a difficult operation, it was found that evidently some animals had been at work on the bones. The major remains recovered of the postcranial skeleton included tibia and fibula portions of the upper part of the vertebral column and some associated rib bones. The tibia showed tooth marks or gnawing.

The find area of the partial remains of Shanidar III in the east wall was re-examined July 31, in the possibility that other bones might be found. In the exploration, several rib bones, vertebrae, and arm bones were uncovered. They lay scattered and broken under a number of stones

between depths 5.15 and 5.40 m. One of the bones was crushed flat under a stone. Stewart observed that the remains suggested to him the presence of the upper part of the torso and parts of the right arm and shoulder. The bones were found in a brown sandy loam-soil fill, in a gap among stones. Several stones lay directly above the bones. This individual must have been sheared across at the torso, since the lower part of the body was found at a lower elevation in the 1957 season.

Shanidar IV was discovered in a cleaning operation. The area where Shanidar I (depth 4.34 m.) was found last season was excavated in depth for any additional data. In clearing the step back of the main pit about 1 m. to the west of the find place of Shanidar I, the leg bones of Shanidar IV were uncovered August 3. It appears that by chance, the excavation of the 1953 and 1956-1957 seasons had halted just at the toes of the skeleton. The skeleton lay flexed on its left side, facing to the west, and head to the south. The top of the skull lay at a depth of 7.49 m. The skull was badly crushed. The skeleton lay in an occupational deposit of loose brown sandy loam soil, next to a large stone that had impeded excavation in the past seasons. The skeleton appeared to be relatively complete, although badly broken and in a friable condition. The bones were somewhat encrusted with a lime coating. They lay close to the stalagmitic horizon, in a zone of moist soil. Stones of small size were found above the skeleton, and some rodent holes were found around the remains. The right hand seems to have been clasped around the left forearm, and the left hand was drawn before the face. Mammal bone fragments and worked flints and raw flakes were found in close proximity to the skeleton. There were no large stones over it, but the skeleton was evidently crushed: it could have been redeposited in its present find position.

On August 8, while in the process of enlarging the excavation preparatory to exploring for possible additional remnants of Shanidar III in the east wall, the broken parts of a fifth skeleton were found. These remains were encountered in the pathway along the east wall that had been cut as an access way to the skeleton of Shanidar I, exposed last season. The new skeleton lay about 1 m. to the south and 50 cm. above Shanidar III. The scattered bones were found at a depth of 4.48 m. below datum. The parts included pieces of the limbs, ribs, and major fragments of the skull. They were rather crushed and broken under stones, in a heavy occupational zone in which were found Mousterian type points and mammal bone fragments. It is our impression that from the way the bones were scattered, either the bones had been disarranged by scavenging animals, or there was some other movement of the bones subsequent to the death of the individual. Fairly large-sized rodent burrows were found around the bones. A few of the bones were found crushed flat under stones, others lay among stones. The top of the skull

was at a depth of 4.39 m. No mandibular fragments were found. Some bone fragments were noted in the excavation wall. These could not be immediately removed this season because of the dangerously heavy overburden of stones. They were left for a fifth season.

In exposing Shanidar IV (meanwhile, Shanidar V had been found), Stewart discovered that there were some extra bones lying to the frost and below Shanidar IV. On August 9, it was evident that there was another skeleton, Shanidar VI, lying somewhat to the east and below Shanidar IV, at a depth of 7.68 m. Both Shanidar IV and VI were removed in a block of earth. It was found that there were some fragments of what is believed to be Shanidar VI in the wall of the cut, lying under heavy overburden. It was determined that it was best to leave these until the following season.

All of these new skeletons discovered this season were found in a space of five days. They were sent to Baghdad, where they will be studied by Stewart. The remains of Shanidar III were forwarded to Stewart in Washington for his study. From the positions of the remains in the field, it appears that Shanidar I and V, lying in the same layer, as well as I could judge, must have been closely contemporary. These individuals were perhaps killed by the same rockfall. Since Shanidar I has been dated about 46,000 years B.P. (Solecki, 1960:629), Shanidar V must be about the same age. Shanidar III, discovered at a lower depth in another soil layer, is undoubtedly older than either, although younger than Shanidar II, IV, and VI. Shanidar IV and VI must have obviously been contemporary, since one was on top of the other. They lay in approximately the same depth as Shanidar II, and may have been in the same cultural layer. Thus we have here too the possibility that Shanidar II, IV, and VI represent part of a population. The Shanidar child, discovered in the 1953 season at a lower depth, is still the oldest of the seven early-man skeletons found in Shanidar Cave.

Paleozoological Studies

Some very interesting new data resulted from the studies of the zoologist of the expedition, Dexter Perkins, Jr. He based his findings on the analysis of the faunal remains from both the cave and the village site. A full report will be published by him. Perkins' analysis as reflected in the faunal remains hints at the beginnings of animal domestication, and a sharp change in economy from a purely hunting and gathering livelihood as evidenced in layers C and D in Shanidar Cave, to an economy in layer B of Shanidar Cave and Zawi Chemi Shanidar in which selective animal breeding is suggested.

This analysis, as Perkins explained at the Rolling Prairie, Ind., conference on May 12 to 14, 1961, shows two shifts in the faunal dependence. The first is that there was a change in dependence from

goats to sheep in the post-Pleistocene ages (from at least 10,800 years ago). The second is that there was a change from a random sample in the age classes of the animals killed to a predominance of young animals less than a year old. Perkins assumes that the occupants of the cave and the village site in the Proto-Neolithic horizon maintained a breeding population over the winter. There is a suggestion from the faunal remains that the cave was occupied during the winter, and the village site during the summer.

Charles Reed of the University of Illinois, Urbana, Ill. had examined the faunal remains of Shanidar Cave and Zawi Chemi Shanidar of previous seasons. From his preliminary analysis, one obtained the impression that the animal remains and other nonartifactual data reflected little climatic change (R.J. Braidwood and Bruce Howe, 1960:163). Perkins has now determined that some changes in size, at least of the goats, is evident in the paleolithic horizons.

Land snails of various types represented a strong element in the diet of the Shanidar post-Pleistocene populations. It is not certain at present whether or not this food, present in small proportions in layers C and D at the cave, is the reflection of a new food habit, or if the population were pressed to supplement their diet with snails under a changing environment. It is certain that snails are found in relatively the same cultural horizon or background across the Near East, and over into northern Africa, as though it were a single cultural habit.

In the general discussion at the Rolling Prairie conference, Reed felt that on the basis of the present evidence from Shanidar, goats and sheep were domesticated before the dog. It is now felt that the dog was not domesticated as early as heretofore supposed according to some authorities.

Paleoclimatology of Shanidar Valley

The ancient climate from the Middle Paleolithic Shanidar D horizon to the post-Pleistocene age and modern times is reflected in fossil pollens and trace elements studies from soil samples at the cave and village site. This is based on the findings of Arlette Leroi-Gourhan of of the Musée de l'Homme, Paris, France, who has studied the fossil pollens, and Bruno Sabels, of the University of California, Berkeley, Calif., who has made a preliminary analysis of the soil samples for trace elements. The latter work was made possible through the cooperation of Richard Shutler, Jr., of the Nevada State Museum, Carson City, Nev. Both Mme. Leroi-Gourhan and Sabels conducted their researches independently, the results of which corroborate each other's findings rather well. The preliminary report of these analyses, entitled, "Paleoclimatology and Archeology in the Near East," by Ralph S. Solecki and Arlette Leroi-Gourhan, will be published by The New York Academy of Sciences

in its forthcoming monograph *Solar Variations, Climatic Change, and Related Geophysical Problems.*

A brief summary of the findings of these two independent investigators follows. The paleobotanical data of Leroi-Gourhan is presented first. This evidence is to my knowledge the only paleobotanical evidence obtained thus far from an archeological site in the Near East. Herbert Wright, Jr., of the University of Minnesota, Minneapolis, Minn. has obtained pollen core samples from Lake Merivan in western Persia, and another lake core sample has been reportedly obtained in Turkey (reported by Wright at the Rolling Prairie, Ind. conference). Leroi-Gourhan has thus far been able to obtain five pollen determinations from layer D, two from layer C, and two from layer B in Shanidar Cave. From the village site, she has obtained three determinations. The nature of the samples restrict the number of pollen grains obtainable, but Leroi-Gourhan has been able to recover enough data to present a picture of fluctuating climate which, coupled with the available carbon-14 dates, affords us a good picture of the environment of prehistoric Shanidar. In the lowest sample (8.6 m. below datum) in layer D, a warm climate is indicated. The fossil pollen include date palms *(Phoenix dactylifera)*, which probably grew in the river valley, about 1000 feet below the cave. No date palms are found in the region today. The second sample (7.5 m.), was collected from just below the skeletal remains of Shanidar II. A very significant cooling of the climate is suggested. Pollen grains include fir *(Abies)*, a cold-loving tree. At the top of layer D, in the neighborhood of Shanidar I at a depth of 4.35 and 4.25 m. were found pollen grains that are botanically similar. They suggest a warm climate, with a hint toward a wetter climate in the upper part of the layer.

The sample from near the base of layer C (4.0 m.) indicates a dry steppe environment. A change is indicated at 3.0 m. depth, with wet and cold climate conditions.

The pollen grains from Shanidar B1 and B2 and Zawi Chemi Shanidar may be considered together since they are botanically rather identical. There is a suggestion of a cooler climate in Shanidar B2, succeeded by warmer conditions in Shanidar B1 and Zawi Chemi Shanidar, to the approximate situation in climate at the present time.

The presence of date pollen in the Mousterian layer is intriguing. As a matter of historic interest, dates were of significance only in the Sumerian civilizations, more than 40,000 years later than the latest of the Neanderthal occupations at Shanidar Cave.

As noted above, Bruno Sabels had made an independent study of the soils for trace elements. He made an analysis of five samples, extending in range from layer A to about the middle of layer D. In layer D, two samples were analyzed. One sample was analyzed from layer C, one from layer B, and one from layer A. His deepest sample, from 8.3 m. in

in layer D, indicates a rather warm climate, corroborating Leroi-Gourhan's findings. The next sample, also from layer D, at 7.3 m., indicates a very cold and moist climate. This also corroborates Leroi-Gourhan's analysis.

From layer C, the sample taken from a depth of 4.85 m., near the base of the layer, suggests cool and humid conditions. No exact parallel is drawn from Leroi-Gourhan's findings from this level. Sabels measured a sample from 2.4 m. in the base of Shanidar B1. His analysis shows that the climate was cooler and more moist than the climate suggested in the more recent sample from layer A. The sample from layer A, at a depth of 1.4 m. suggests a climate similar to the present, with no pronounced aridity.

In summary of this section, we seem to have the first reliable record of paleoclimate in the Near East, combined with archeological data and based upon carbon-14 dates. It is expected that there will be additional refinements upon the present set of data as research progresses on the study of Shanidar soil samples.

Conclusion

Interdisciplinary studies in anthropology are now the rule instead of the exception. We follow the rule here. We expect that when all of the various data are combined we shall have an interesting picture to illustrate the life of prehistoric peoples in Shanidar valley from cave to the beginning of village life.

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DIVISION OF BIOCHEMISTRY

A BIOCHEMICAL APPROACH TO CHEMOTHERAPY*

George H. Hitchings

Wellcome Research Laboratories, Burroughs-Wellcome and Company, Inc., Tuckahoe, N. Y.

The conventional program in chemotherapy consists largely in more or less random testing of chemical compounds in screening tests that resemble somewhat closely the human disease for which it is hoped to find a cure. The program to be discussed herein has had as its primary objective the production of antimetabolites that would cause specific biochemical lesions. A number of these have found chemotherapeutic applications, some by design and some empirically. However, even in those instances where an application has been found by random testing, the biochemical approach has been of value since it has resulted in agents with rather well defined *loci* of action. The ability thus to deal with reaction mechanisms has been of prime importance to the ultimate usages of the substances.

Nucleic acid biosynthesis was chosen as a field because it appeared probable that exploitable biochemical differences between host and parasites, both qualitative and quantitative might exist among these mechanisms. Each of the natural purine and pyrimidine bases was studied in turn. The significance of each chemical feature was investigated by studying the effects of chemical variation upon the response of a model biological system, *Lactobacillus casei*.[1-5] This has provided a reference chemical-biological correlation that often has greatly simplified the task of relating structure to activity when new biological systems were investigated. A small segment of this program has been chosen for discussion here as an illustration of the program as a whole.

One of the early findings was the discovery that essentially all derivatives of the 2,4-diaminopyrimidine system possess antifolic acid activity.[6] This discovery arose from observations on the anomalous behavior of the 2,4-diamino analogue of the nucleic acid base, thymine. This substance replaced thymine for the growth of *L. casei* in the presence of purine and absence of folic acid, but when the organism was grown in the presence of folic acid alone, it was an inhibitor of growth.[4] Observations on variants of this molecule resulted eventually in the synthesis of a large family of small molecule folic acid antagonists, a number of which have found applications in chemotherapy.[7]

Folic acid is a B vitamin of ubiquitous occurrence and is a dietary essential for many animal species. It exists in two primary states, with

*This paper, illustrated with slides, was presented at a meeting of the Division on May 23, 1961.

the pyrazine ring in the aromatic form or in the tetrahydro state. Tetrahydrofolic acid itself is unstable and usually exists only as one of its derivatives in which the N_5 or N_{10} atom or both are substituted with a one-carbon moiety such as formyl, hydroxymethyl, or methyl. Further variants are provided by variations in the number of amino acid residues attached by peptide linkage to the glutamyl residue, so that in natural products a multiplicity of factors is detectable. The natural coenzymes presumably are mainly triglutamates,[8] but the monoglutamates serve as well or nearly as well in the enzyme systems that have been studied. These coenzymes participate in the transfer of the one-carbon moieties to suitable precursors as shown in FIGURE 1. Thus two different coenzymes are involved with two steps in the biosynthesis of the purine ring, an additional one with the methyl group of thymine and still another with the methyl group of methionine.[8,9]

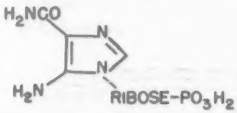
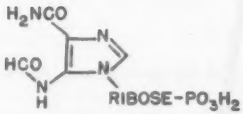
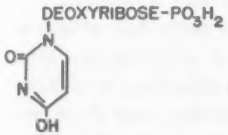
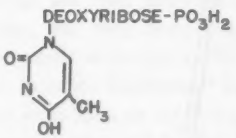
Precursor	Product	Coenzyme
CH_2NH_2 | $CO-NH-RIBOSE-PO_3H_2$	$CH_2-NH-CHO$ | $CO-NH-RIBOSE-PO_3H_2$	N_5, N_{10}-methenyl THFA
		N_{10}-formyl THFA
		N_5, N_{10}-methylene THFA
$H_2NCH_2CO_2H$	$HOCH_2CH(NH_2)-CO_2H$	N_5, N_{10}-methylene THFA
$HSCH_2CH_2-CH(NH_2)CO_2H$	$CH_3SCH_2CH_2-CH(NH_2)CO_2H$	N_5-methyl THFA

FIGURE 1. Reactions involving coenzymes derived from folic acid. Precursors, products, and the appropriate one carbon substituent of the tetrahydrofolic acid (THFA) to form the coenzyme are shown.

The reduction of folic acid appears to be a necessary step in the biosynthesis of these derivatives of tetrahydrofolic acid, or else a reversible oxidation-reduction may be involved in their utilization. In either case it is now clear that a wide variety of species is intoxicated by the so-called antifolic acids and that the action of these antimetabolites is primarily an inhibition of folic acid reductase.[10]

The metabolite-antimetabolite relationships of a typical antifolic acid are shown in FIGURE 2. It will be observed that for the growth of *Streptococcus faecalis*, folic and folinic (*N*-5-formyltetrahydrofolic) acids are essentially equivalent. However, in the presence of very small concentrations of a folic acid antagonist such as pyrimethamine strong inhibition is observed when folic acid is proffered, but the growth with folinic acid is unaffected until concentrations of the inhibitor some 500-fold greater are reached. It is noteworthy that both with folic and with folinic acid, there is a narrow concentration range in which the inhibitor and the nutrilite appear to be competitive. However, the primary action of the antagonist is clearly an interference with the conversion of folic acid to folinic acid, that is, with the action of folic acid reductase.

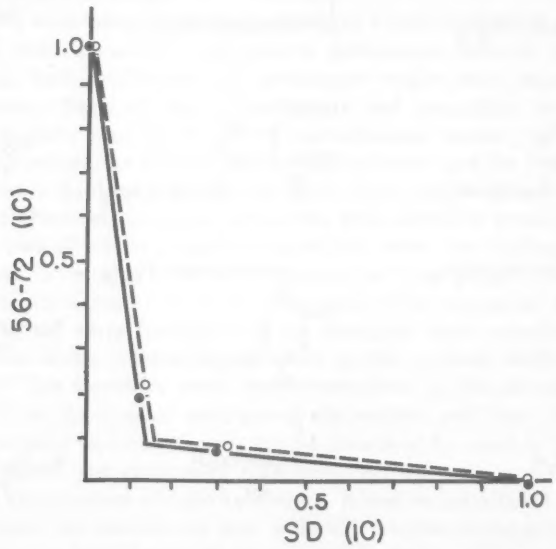


FIGURE 2. Potentiation in combinations of trimethoprim (B.W. 56-72) and sulfadiazine (S.D.) in the treatment of *Proteus* infections in mice. The units on the axes represent the doses (I.C.) of the individual drugs required to produce half the maximum per cent survival, and hours survival. Each point on the graph represents a combination of fractions of these doses of the two drugs: ———per cent survived; - - - - - hours survival.

With pyrimethamine the difference in inhibition index (ratio of antimetabolite to metabolite for half-maximal growth) between the growth with folic acid and that with folinic acid is very wide indeed. The ratio between these indices may be regarded as a measure of the prominence of the effect on folic acid reductase in the total picture of inhibition. This varies from compound to compound (TABLE 1). It is noteworthy that the structural analogues of folic acid, A-Methopterin and aminopterin in this respect fall within the range exhibited by other pyrimidine derivatives but, as will be shown, these substances differ markedly from the small molecule antifolic acids in their chemotherapeutic effects.

TABLE 1

SUPERIORITY OF FOLINIC OVER ACID FOR REVERSAL OF INHIBITIONS PRODUCED BY 2,4-DIAMINO DERIVATIVES

	I_{CF}/I_{FA}
5-*p*-Chlorophenyl-6-ethylpyrimidine	500
A-Methopterin	125
Aminopterin	30
6-Chloroquinazoline	50
5-(3,4,5-Trimethoxy benzyl)	30
5,6-Dimethylpyrimidine	35
5,6-Cyclopentenylpyrido(2,3-d)pyrimidine	25
6,7-Dimethylpteridine	15
Purine	15
8-Azapurine	2

I_{CF} — The ratio of inhibitor to leucovorin required to produce a 50 per cent inhibition of growth.

I_{FA} — The corresponding ratio using folic acid.

Aminopterin and A-Methopterin are best known for their effects on leukemia and other malignancies, but they show little effect on bacteria and protozoa. A few of the small molecule antifolic acids are also capable of producing remissions in acute leukemia,[11] but as a group they are much more notable for their activities on microorganisms. An analysis of the biochemical differences involved in the various responses to the two types of antifols serves to explain not only the difference in response of various unicellular species, but also the differential toxicity between host and parasite that exists for the many of these compounds.

The reasons for these differences reside in species differences in the biochemical pathways to the coenzyme forms of folic acid and in the cellular transport mechanisms. Generally speaking, folic acid (or its intracellular equivalent) is formed in one of two ways in nature. Either it is synthesized *do novo via*, a mechanism that involves *p*-aminobenzoic acid, or it is incorporated from exogenous sources. Only a few excep-

tional organisms have the capacity to do both.[12] Moreover, the uptake of folic acid appears to be an active concentrative process, at least it requires energy and is inhibited in the cold. As might be expected the close structural analogues of folic acid are taken up by cells in much the same way as folic acid itself.* The small molecule antifols, on the other hand, appear to enter cells by a process of passive diffusion. Their uptake is not markedly influenced by temperature, and is not only not favored by the presence of glucose but may actually be inhibited. It is apparently for these reasons that the majority of unicellular organisms are inhibited by one or more of the small molecule antifols but are not inhibited by aminopterin.

In addition to uptake, a second factor involved in differences in behavior of one species to the various drugs and differences in response of different species to the same drug may lie in the relative binding of the various folic acid reductases. This possibility has not been explored directly. However, it is known that aminopterin and A-Methopterin combine with folic acid reductase from mammalian sources almost irreversibly.[10] The binding of the small molecule antifols to the mammalian enzymes appears to be much less, and in some cases nil,** although corresponding enzymes from bacteria are strongly inhibited.

A third factor involved in the differential toxicity, is the capacity of the various species to by-pass the biochemical block imposed by the drug. Since man can incorporate citrovorum factor, which is beyond the metabolic block imposed by the antifols, whereas most of the unicellular parasites cannot, the therapeutic index of many of the antifolic acid drugs can be substantially increased when they are given together with leucovorin. This will be illustrated below.

A fourth element may be brought into the problem of differential toxicity. Many microorganisms synthesize folic acid *via* a pathway that involves *p*-aminobenzoic acid and are sensitive to sulfonamides, which compete with the latter for the synthesis of folic acid. These biochemical reactions, however, are lacking in the host and whatever toxicities the sulfonamides exhibit in man are quite unrelated to their major biochemical effects. As a consequence of the sequential arrangement of the biochemical blocks when a sulfonamide and an antifol are used simultaneously, the toxicity for susceptible microorganisms is greatly enhanced, while that for the host remains essentially unaltered. This is illustrated in FIGURE 2 which shows the results of therapy of *Proteus* infections in mice with a combination of sulfadiazine and 5-(3,4,5-trimethoxybenzyl)-2,4-diaminopyrimidine(trimethoprim). Each point on the graph represents an amount of drug or drugs sufficient to protect 50

*A few organisms such as *L. arabinosus* and *B. subtilis* appear to assimilate aminopterin by mechanisms other than those involved with folic acid.[12-15]

**For example, no signs of folic acid deficiency in growing rats by high, long continued dosing with either of two alkoxybenzylpyrimidines (unpublished experiments).

per cent of the animals. This is termed the inhibitory concentration (I.C.) for the individual drugs. The figure shows that when the two drugs are used in combination, protection is obtained with small fractions of these I.C.'s. Thus approximately 0.2 I.C. of trimethoprim + 0.1 I.C. of sulfadiazine or 0.1 I.C. of trimethoprim + 0.3 I.C. of sulfadiazine is sufficient to provide protection as great as a full I.C. of either substance alone. TABLE 2 provides another illustration of potentiation in a similar combination, in this case pyrimethamine,[17,18] plus sulfadiazine in the treatment of murine toxoplasmosis. Here it is seen that sulfadiazine extends survival but provides no cures. With pyrimethamine alone at maximal dosage about half the animals were cured. With a combination of a half-dose of sulfadiazine and a one-third dose of pyrimethamine, all were cured. This table illustrates another point that was mentioned above, that is the possibility of improvement of the chemotherapeutic index by the simultaneous administration of a substance that will counteract the toxicity for the host without at the same time affecting the results of therapy. It is seen that when various metabolites are given along with the drugs, the results are about as expected. Thus *p*-aminobenzoic acid reduces the effectiveness of the combination, and can be regarded as antidotal to sulfadiazine for the parasite. On the other hand, folinic acid, which is known to protect the host against the toxicity of pyrimethamine,[7] does not interfere with the chemotherapeutic activity of the combination.

TABLE 2

EFFECTS OF DRUGS AND VITAMINS, SINGLY AND IN COMBINATION ON EXPERIMENTAL MURINE TOXOPLASMOSIS[16]

	Survivors	Sulfadiazine 60 mg. %*	Pyrimethamine 100 mg. %	Sulfadiazine + pyrimethamine 30 + 30 mg. %	None
None	15 day	8	10	10	0
	30 day	5	7	10	0
	Cured	0	5	10	0
PABA	15 day	0	5	10	0
100 mg. %	30 day	0	0	9	0
	Cured	0	0	8	0
Folic	15 day	2	9	10	0
60 mg. %	30 day	2	5	10	0
	Cured	0	4	10	0
Folinic	15 day	8	10	10	0
6 mg. %	30 day	5	9	10	0
	Cured	0	2	10	0

*Numbers indicate mice surviving in treatment groups of 10 each. Dosages refer to mg./100 gm. of food.

The possibility of imposing a third block on the same biochemical pathway with the aim of producing a further potentiation, also has been explored.[20] Using analogues of end products of the various systems that involve folic-acid-containing coenzymes, it has been possible to show additional potentiation with a third block. This is illustrated in TABLE 3. Here there were determined the inhibitory effects of 5-(3,4-dimethoxybenzyl)-2,4-diaminopyrimidine, sulfadiazine, and 8-azaguanine on the growth of *Proteus vulgaris in vitro*. It is seen that in various combinations of two of these drugs the amounts required to inhibit are significantly less than expected on the basis of additive effects, and that when all three are used a further greater-than-proportional reduction is achieved.

TABLE 3

THE EFFECTS OF COMBINATIONS OF THREE BIOCHEMICALLY-RELATED ANTIMETABOLITES ON THE GROWTH OF *PROTEUS VULGARIS*

Compound	Concentration for 50% inhibition μg./ml.		
	A	B	C
8-Azaguanine	26	–	–
Sulfadiazine	–	1.9	–
B.W. 49-210	–	–	2.2
B + C	–	0.23	0.39
A + B	1.6	0.035	–
A + C	5.6	–	0.29
A + B + C	2.1	0.06	0.10
	0.5	0.21	0.03
	0.8	0.02	1.40

These results may be taken as support for the view that it is worthwhile to seek still further blocking agents on the pathways to nucleic acid biosynthesis. Antimetabolites have been forthcoming only for the *p*-aminobenzoic acid moiety of folic acid, and little is known about the origins of the pteridine moiety, although it is clear that some bacteria at least can couple a pteridine with *p*-aminobenzoic or *p*-aminobenzoylglutamic acid to produce folic acid.[21,22] Since a clear-cut qualitative difference exists between man and microorganisms in the synthesis of folic acid, this would appear to be an exploitable biochemical difference. There is growing evidence that many cells become resistant to the action of antifolic acid drugs through the synthesis of greatly increased amounts of folic acid reductase.[23] This escape from inhibition might be overcome if one had antagonists specific for the individual coenzyme forms of folic acid. This is a field that has scarcely been touched, although it recently has been suggested that tetrahydroaminopterin is an antagonist of the 5,10-methylene tetrahydrofolic acid. In any case, it is obvious that the biosynthetic pathways leading to the nucleic acids and

related substances still provide many opportunities for further exploitation toward new chemotherapeutic agents.

One has heard a great deal about the need for, and the possibility of, a rational chemotherapy. In the minds of some, chemotherapy would be rational only when new agents could be produced on demand, fully formed, like the heroes who arose from the dragon's teeth of Jason. Perhaps this rational chemotherapy will arrive in one glorious stroke of genius. It seems more likely, however, that it will arrive by small increments of progress and for this reason unheralded. When one looks back over the past 20 years it is possible to conclude that a great deal of progress has been made. Perhaps the most important development is the breaking down of the artificial barriers that previously existed between enzyme studies on the one hand and studies directed toward chemotherapy on the other.

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DIVISION OF MICROBIOLOGY

DISINFECTANTS, ANTISEPTICS, AND PRESERVATIVES*

Philip C. Ersman

Research Department, CIBA Pharmaceutical Products, Inc., Summit, N.J.

As the title of my paper suggests, this discussion is confined to a general consideration of the means by which we eliminate microbes from medicinals and other objects that bear directly or indirectly upon our well-being. The subject of chemotherapy, which deals with the treatment of established infectious diseases, is much too large and will not be considered here. It must be borne in mind, however, that certain substances can serve either as preservatives or disinfectants or even as chemotherapeutic agents. For instance, the quaternary ammonium compounds are excellent antiseptics when applied to the skin and yet are considered effective, chemotherapeutically, in the treatment of skin infections and sore throats. The tetracycline antibiotics are active not only in combating established infections, but are most useful as preservatives in extending the shelf life of dressed poultry and fish, as well as packaged vegetables and fruits.

Historical

There is evidence that an empirical knowledge of preservatives developed early, for at the dawn of recorded history, drying, salting, and smoking were common practices, and spices, wines, vinegars, and aromatic oils, for such purposes, were highly regarded. The ancient Egyptians believed that the preservation of the body was essential for a happy life hereafter and, by trial and error they attained considerable knowledge in the preservation of their dead. That their methods, which involved the use of resins, naphtha, and liquid pitch, were effective is proved by the large number of mummies that still remain in an excellent state of preservation.

Probably because of superstition, the ancient Persian laws directed that drinking water be kept in bright copper vessels. Today we know that water kept in such containers soon becomes sufficiently germicidal to kill most of the bacteria capable of causing water-borne intestinal infections. The Bible gives detailed instructions as to the methods to be used in the quarantine, cleansing, and anointing of lepers, as well as directions for the purification of houses that had sheltered individuals ill with this and other diseases. There are many other examples of the very early use of disinfecting agents, all during the period when the very existence of microbes was not to become known until many centuries later.

It is recorded that when the Great Plague swept Europe during the

*This paper, illustrated with slides, was presented at the meeting of the Division of Microbiology on May 26, 1961.

Middle Ages, John of Burgundy issued instructions that the air in rooms occupied by the victims be purified by burning juniper branches, and that powders be thrown on the coals to provide fumes for the patients to inhale. It is entirely conceivable that such vapors may have had some value as germicidal inhalants against the pneumonic form of plague.

Attempts at disinfection, although necessarily conducted upon an empirical basis, were especially numerous from the beginning of the 19th century. For example, the relation of unclean water and unsanitary dwellings to the spread of disease was recognized by Catbush in 1808, who directed that the drinking water be treated with quick lime and that the sleeping quarters on ships be frequently whitewashed with lime. In 1827, Alcock,[1] writing in the British medical journal *The Lancet*, emphasized the disinfectant properties of the hypochlorites and, needless to say, was roundly attacked by his contemporaries for these "heretic" views. The virtues of chlorine water as a disinfectant were extolled by Lefevre[2] in 1843, who also directed attention to the fact that puerperal sepsis was contagious. Three years later, Semmelweis employed chlorine to nullify the so-called "cadaveric poisons" carried on the hands of physicians.

Without citing other instances in which phenol, silver nitrate, iodine, and potassium permanganate, among others, were advocated in the war against disease, we can already see that both popular and scientific thought was being prepared for the acceptance of the discoveries of Pasteur and Koch.

In 1881, Koch[3] introduced an exact method of comparing the bactericidal power of various substances. Instead of working with fluids swarming with different microorganisms of varying resistance, he tested the action of these compounds on pure cultures of bacteria of approximately equal resistance. By drying anthrax spores on silk threads of the same length, immersing them in a solution of the substance to be tested, and subsequently transferring them to a nutrient broth in order to ascertain whether the bacteria were still alive, he collected a considerable quantity of data on the relative merits of different disinfectants. In a now classic paper published in 1897, Kronig and Paul[4] described a method for the quantitative study of disinfection involving garnets coated with spores and plating for survivor counts, and thereby demonstrated, for the first time, that in a culture subjected to the influence of a germicidal agent, bacteria die, not simultaneously, but in an orderly sequence. It was not long after, that Madsen and Nyman[5] showed that the law underlying the death of bacteria is similar to that governing a simple monomolecular chemical reaction. This is indicated in FIGURE 1, in which is shown the logarithmic order of death of a typical bacterium.

Definition of Terms

After using such terms as preservative, disinfectant, and germicide, it is appropriate that the various expressions one encounters in any dis-

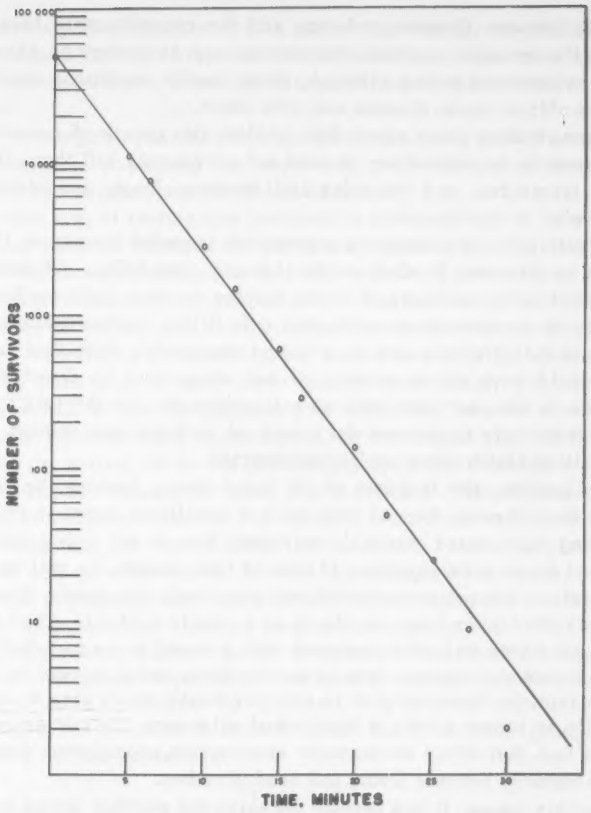


FIGURE 1. Survival curve: log survivors plotted against time of exposure.

cussion dealing with preservation and disinfection be defined. A confusion of terms has indeed grown around the process of killing microorganisms and if, in turn, I confound this confusion even further, at least I shall do so with an air of authority.

The words disinfectant and antiseptic appeared in English writing about the start of the 17th century. These expressions were used to denote rather vague ideas and, even today, they are often used in general rather than precise meanings. The suffix cide is added when killing is meant, while stasis is added when the multiplication of microorganisms is prevented. Stat is used as a suffix when referring to an agent producing the condition of stasis as in the case of a preservative.

A disinfectant destroys infectious microbes, and disinfection is the act of killing them. Actually the term disinfectant applies to both infectious and noninfectious germs, since bacteriologists now realize that the

division between disease-producing and the nonpathogenic bacteria is vague. For example, certain streptococci may be present in the normal throat as harmless guests although, under certain propitious conditions, they are able to cause disease and even death.

A preservative is an agent that inhibits the growth of microbes and thus prevents decomposition: it need not necessarily kill them. Bactericides, fungicides, and virucides kill bacteria, fungi, and viruses, respectively.

An antiseptic is in essence a germicide intended for use on the skin or as a mouth wash. In other words, it is any germ-killing substance that is applied to the surfaces of living tissues or skin. Such products may properly be considered as antiseptics only if they destroy bacteria in the recommended dilutions and in a period comparable with that in which they would have an opportunity to act when used as directed. Many products in the past were sold as antiseptics despite the fact that they barely were able to prevent the growth of bacteria and, indeed, had no germ-killing ability when applied as directed.

Sterilization, the broadest of all these terms, denotes the complete destruction of every form of life. Thus a sterilizing agent is capable of rendering the treated material completely free of all living organisms. Fire and steam under pressure, if applied long enough, as well as certain chemicals in adequate concentrations, are sterilizing agents. When dealing with the higher forms of life, it is a simple matter to prove that life no longer exists following treatment with a sterilizing agent. With regard to the microbes, however, this is not the case, and it is only by indirect means that the bacteriologist is able, or thinks he is able to establish that life no longer exists in the treated substance. This is necessitated by the fact that direct microscopic examination cannot even distinguish with assurance between living and dead microbes.

For this reason, it has become the universal practice among microbiologists to assume that a microbe is dead if it fails to multiply when transferred to nutrient broth. While it is obvious that a dead germ cannot possibly multiply, it is by no means correct to infer that one incapable of multiplication in the fresh broth is dead. Until recent years, it was believed that under proper conditions of time and intensity of exposure, ultraviolet rays were capable of killing many varieties of microorganisms as evidenced by their inability to multiply later when transferred to broth. It remained, however, for Kelner[6] to show that recovery of so-called killed phages of *Escherichia coli* and *Streptomyces griseus* may occur upon their exposure to ordinary light.

Again, if bacteria previously exposed to a germicide are washed free of the adsorbed agent and then transferred to nutrient broth, growth may take place, depending upon the rinsing procedure. Such observations indicate the possible reversibility of a poisoning mechanism. The ability of mercurials to inhibit growth of bacterial cultures is so striking that it has created the assumption of high disinfecting potency. This belief

was severely shaken when it was shown that the growth-inhibited bacteria resumed lusty growth when the adsorbed mercurial was neutralized by the mere expediency of adding -SH-containing compounds to the culture medium.

These foregoing remarks should indicate the shaky ground upon which we tread when assessing the sterilizing potentialities of the various chemical and physical agents of disinfection.

Another area of testing that involves an interpretation as to whether a particular solution intended for parenteral use, that is, by injection, is free of viable organisms is the sterility test. Such products, in order to be considered sterile, must be shown to contain no living microbes when transferred to suitable nutrient media. The surest way to demonstrate sterility therefore is to transfer *all* of the material to a suitable quantity of broth. This type of destructive testing is obviously ridiculous, for nothing would be left for ultimate use. Within the bounds of scientific validity and governmental requirements, good business practice therefore calls for the setting aside, for the sterility test, of a minimum number of vials or ampuls. Bearing in mind that the U. S. P. recommends no less than 10 containers be tested for sterility from each autoclave load or filling operation, let us consider the scientific basis that presumably justified this recommendation. In 1949, Knudsen,[7] a statistician, published a most interesting and, one may add, disturbing report on the shortcomings of the sterility tests as recommended by the U. S. P. Her findings are summarized in TABLE 1. So disturbing were these findings that, today, manufacturers of products sterilized by means other than heat, as for example those sterilized by filtration, test at least twice the number of recommended samples from each batch. However, even going to that extreme is not too trustworthy.

TABLE 1*

CHANCES OF PASSING DEFECTIVE LOTS AS RELATED TO SAMPLE SIZE

Percentage Defective in lot (Percentage of contaminated units in the lot)	Chances of passing lot after testing sample of size:		
	$n = 10$	$n = 15$	$n = 20$
5	60 out of 100	45 out of 100	35 out of 100
10	34 out of 100	20 out of 100	11 out of 100
15	19 out of 100	8 out of 100	4 out of 100
20	10 out of 100	3 out of 100	1 out of 100
30	2 out of 100	5 out of 1000	1 out of 1000

*Reproduced from L.F. Knudsen[7] by permission of the *Journal of American Pharmaceutical Association.*

I have purposely discussed sterilization and the sterility test at some length only to emphasize the fact that we do not always have the means to prove that all microbes in a specific instance have been completely and totally destroyed, and that the term sterility, as applied to any product, is often only a prayer and a hope.

Another term that warrants some discussion is bacteriostasis. It should be pointed out that certain compounds referred to as disinfectants actually exert only bacteriostatic action. These are the dyes and sulfonamides. In other instances, however, it has been well established that there is no sharp differentiation between mere inhibition of bacterial growth and germicidal action. Actually such a separation is made only for convenience. The general relationship between these two activities is clearly demonstrated in a disinfection spectrum such as the one devised by Marshall and Hrenoff[8] and shown in FIGURE 2.

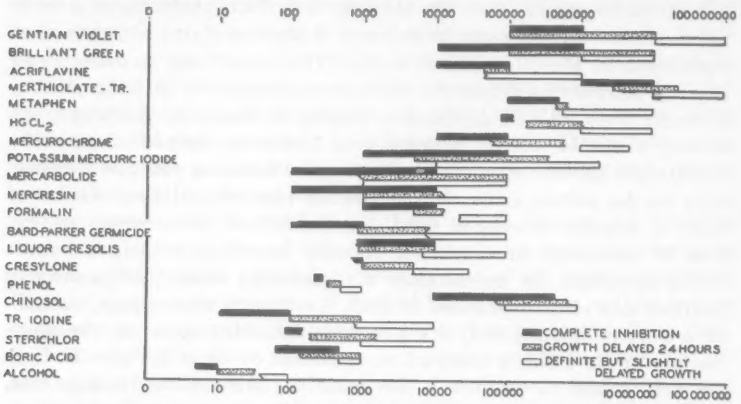


FIGURE 2. Bacteriostatic ranges of 20 disinfectants. Average data for six organisms. Reproduced by permission of the *Journal of Infectious Diseases*.

The bars of the chart are drawn from data obtained with six representative microorganisms inoculated in broth containing various dilutions of the disinfectants tested. The activity of each substance has been divided into three ranges: (1) that depicted by the solid bars, representing dilutions that permitted no growth during the observation period; (2) the range indicated by the stippled bars, designating the dilutions in which growth was delayed only for 24 hours, with growth developing thereafter, and (3) the category of dilutions representing demonstrable inhibition, but in which multiplication occurred in less than 24 hours. Although not indicated in this chart, a fourth range, the bactericidal zone, can be superimposed upon the solid bars. Were one to transfer a loopful of the broth containing all those dilutions of the disinfectant that completely inhibited growth into fresh broth, one would find that, at some point to the left, subculture growth would not take place. This point will represent the highest dilution in which bactericidal activity occurs. The gradual merging of a bacteriostatic effect into a bactericidal one has been generally interpreted to mean that the mechanisms of the two effects are similar and differ only in a quantitative way.

One can add a fifth band to the spectrum shown in this chart, which would extend to the right of the open bars. An interesting aspect of poisonous substances is their universal tendency to *stimulate* rather than depress biological processes leading up to bacteriostasis, a phenomenon also known as the Arndt-Schultz law. Invariably the stimulatory concentrations are slightly less than the minimum harmful concentration.

It would seem appropriate to follow up with a discussion of these remarks, certain of the more interesting agents now used to diminish or completely eliminate bacterial populations found in pharmaceutical preparations, in foods, and on the skin: to mention only three important areas where such effects are most desired.

TABLE 2, in summary form, indicates the commonly used physical and chemical agents that achieve this effect. For convenience, I have distinguished between heat, in its various forms, from all other procedures regardless of whether they represent physical or chemical agents.

TABLE 2

METHODS AND AGENTS FOR ACHIEVING STERILIZATION, DISINFECTION OR PRESERVATION

Heat: Steam under pressure, dry heat, fire, pasteurization.

Nonheat:

(1) *Physical agents:* Filtration, ultraviolet radiation, X rays, radioactive emanations, cathode rays, supersonic vibrations.

(2) *Chemical agents:*

(a) Gases: Formaldehyde, ozone, ethylene oxide.

(b) Others: Synthetic detergents; alcohols, acids and alkalies; phenols; metallic compounds; halogenated compounds; *p*-hydroxybenzoic acid esters, and certain antibiotics.

Heat

We need but devote a few words regarding heat as a means of destroying microorganisms. There is no more effective way to be rid of these forms than by subjecting them to high temperatures. It is obvious, however, that the use of heat is generally limited since many materials including a number of pharmaceutical preparations, plastic tubing used in disposable equipment for intravenous administration of sterile fluids, and many other objects cannot withstand such treatment.

Filtration consists of the passage of fluids through filters consisting of porous clay, porcelain, asbestos, diatomaceous earth, or sintered glass. The pores of the filter must be small enough to prevent the passage of all bacteria and fungi likely to be present in the liquid. The term filterable viruses arose from the fact that none of the bacteriological filters was capable of retaining the viruses. To prepare a filter of pore size such that viruses can be held back would entail an extremely slow

process of filtration and render the process extremely impractical. In addition to pore size, the adsorbing characteristics of the filter material *p*H, electrical charge of the material being filtered, temperature, pressure, and duration of the filtration process all play important roles in the efficiency of filtration.

We now come to another group of important physical forces that adversely affect microorganisms: the electromagnetic waves. As indicated in FIGURE 3, certain ranges of the electromagnetic spectrum possess bactericidal properties.

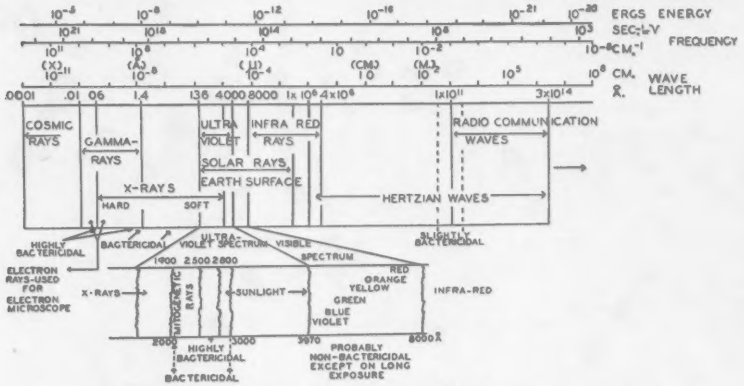


FIGURE 3. The known bactericidal regions of the electromagnetic waves.

Of all these radiations, the gamma and ultraviolet rays are undoubtedly of greatest bactericidal activity. Certain of the Hertzian waves and even those of the visible spectrum under certain conditions are slightly bactericidal. Whether all these various rays bring about their harmful effects by producing secondary toxic substances such as ozone or hydrogen peroxide, alter cell permeability, or bring about protein coagulation within the cell has not been definitely proved. It is believed by some that the radiations to the right of the visible spectrum produce their effects by means of heat produced in the materials being treated, while the radiations to the left of visible light are bactericidal not by virtue of heat production, but as a result of direct hits by the radiations on the target. It is these latter radiations that produce their effects without heat that one has in mind when referring to cold sterilization.

Ultraviolet Irradiation

Investigations on the germicidal effect of ultraviolet rays indicate that the band between 2400 and 2700 Å units is the most active. All types of microorganisms are, in general, affected to the same extent, in that plots of the logs of the survivor count against time of exposure generally yield straight lines indicative of a monomolecular reaction.

However, taking into consideration variations in the susceptibility of individual organisms because of differences in age and metabolic activity, ultraviolet irradiation cannot always be relied upon to produce a 100 per cent kill in the material being treated. For this reason and because these rays cannot penetrate into solids to any important extent, ultraviolet light is used primarily in so far as the biological and pharmaceutical industries are concerned, for the elimination of air-borne microorganisms and, in particular, in areas where the filling of sterile products is being done.

Several years ago we were confronted at our plant with successively contaminated batches of a nasal solution, notwithstanding the incorporation into this product of a usually adequate concentration of merthiolate. In the course of our investigation, it became apparent that the stored, demineralized water used in the preparation of this product contained an inordinate number of pseudomonads of the same type found in the product. The problem was solved by the simple device of emptying the storage tank at frequent, regular intervals. However, to safeguard the product fully, an ultraviolet sterilizing unit was installed in the pipe leading from the water storage tank to the mixing tank. To illustrate the effectiveness of this ultraviolet treatment, I have gathered some data that appear in TABLE 3.

TABLE 3
EFFECT OF ULTRAVIOLET TREATMENT OF STORED DEMINERALIZED WATER ON BACTERIAL CONTENT

	Building M		Building U	
Date	Before	After	Before	After
11-6-57	>5000	52	1500	<10
11-20-57	>5000	27	30	<10
12-11-57	2000	<10	135	0
1-8-58	>5000	54	27	<10
1-15-58	1300	68	200	<10
2-26-58	780	<10	104	<10
3-5-58	2300	0	250	32
3-19-58	>5000	10	820	0

Although I have stated that ultraviolet light is of uncertain value in the sterilization of pharmaceutical or biological products, some limited experiments have been made on its effects on the antigenic properties of bacteria and viruses used in vaccines. In dealing with cultures consisting of cells of uniform age and sensitivity – as in the case of manufacturing vaccines – there is increasing evidence that ultraviolet-inactivated cell suspensions are more antigenic than heat or chemically treated lots. Such inactivated cells have permanently lost their ability to multiply but are otherwise alive. Outright killing of these organisms by prolonged irradiation results in an appreciable loss in antigenicity and the products is of little value as a vaccine.

Cathode Rays

These rays coincide approximately with the gamma and hard X-ray bands in the electromagnetic spectrum. These rays consist of electrons accelerated by man-made machines, and they appear to have practical importance in the sterilization of a variety of materials, including frozen human explants intended for grafting.

The acceleration of electrons for the production of cathode rays is accomplished by three types of equipment of which the best known one is the Van de Graaf electrostatic accelerator. As already mentioned, the cathode ray method of sterilization may be applied to an extremely wide variety of materials, including foods, pharmaceuticals, and biologicals, as well as medical and surgical supplies. Since the heaviest dose required to destroy the most resistant spore or virus produces a temperature rise of not more than 5° C., this method has been used even for the sterilization of frozen tissue, bone, cartilage, and blood vessels freshly removed from cadavers and intended for transplantation to the living.

Although studies have shown that certain drugs sterilized by these rays as, for example, penicillin, streptomycin sulfate, testosterone, and others, have suffered no loss in biological activity, this is not the case with other products, as is shown in TABLE 4. Flavors, in the case of treated foods, are said to be unaffected, but this point is debatable. Discoloration may occur in some materials and also in most types of clear glass containers, which become amber in color.

TABLE 4

EFFECT OF CATHODE RAYS ON PHARMACEUTICALS

Product	Dosage (rep × 10^6)	Loss in potency after irradiation
K penicillin	4.1	No loss
Ergotrate	4.1	50%
Thromboplastin	4.1	100%
Insulin	0.1	100%
Thiobarbiturate	4.1	Slight loss
B complex & Vitamin C	4.1	No loss

It is only natural, in order to sterilize effectively all of the items mentioned, that the cathode rays, without exception, exert a killing action on all varieties of microbes. This activity is indicated in TABLE 5, which is a partial listing of the organisms tested by Brasch and his group[9] with the Capacitron. The energy carried by the electrons is the prerequisite for obtaining the desired biological effect. The energy of electrons released in biological materials is conveniently expressed by a unit that has been called roentgen equivalent physical or rep, which is a measure of the amount of energy absorbed within one gram of the absorber. The doses are indicated in terms of rep. As indicated in this table, several hundred thousand reps are required to destroy these various microorganisms.

TABLE 5*

100 PER CENT STERILIZING DOSES (REP) FOR VARIOUS MICROBES WITH HIGH INTENSITY ELECTRON BURSTS

Nonsporeformers		*Viruses*	
S. hemolyticus	200,000	Polio (Lansing)	1,600,000
E. coli	100,000	Rabies	850,000
Pseudo. aeruginosus	100,000	Influenza	800,000
S. aureus	200,000		
Sporeformers		*Phages*	
Cl. tetani	400,000	*E. coli*	650,000
B. antracis	500,000	Flexner I	650,000
Cl. welchii	250,000	Staph. V	600,000

*Reproduced by permission of A. Brasch *et al.*[9] from the *Proceedings of the Rudolf Virchow Medical Society.*

Perhaps one of the reasons why cathode-ray sterilization is not universally applied is the extremely high initial cost of the equipment and its maintenance. The Van de Graaf machine costs at least $400,000. Perhaps the only practical purpose for which such costs are justified is in connection with the sterilization of very large batches of bandages, sutures, and similar materials.

Chemical Agents

Having discussed what I believe to be the more important physical means of sterilization, let me now turn to the chemical agents with which we are more familiar.

Since formaldehyde and ozone are two gases that are of little practical importance, we shall proceed directly to a gas that has demonstrated great utility.

Ethylene oxide (FIGURE 4) first assumed importance as a sanitizing agent in 1928, when it was described as a powerful insecticide.[10] In 1936 its activity as a fungicide was recorded, and the first spectacular use of ethylene oxide gas in this connection was the treatment of wrapped, sliced bread.[11] Some of you may recall that when sliced bread was first introduced, its shelf life was indeed a very short one because of the development of mold. This was due, in spite of all attempts at disinfection, to the heavily contaminated slicing machines. By placing the wrapped bread in large chambers, drawing a vacuum of about 28 inches of mercury and then introducing the gas until the proper pressure was attained, a most troublesome problem was solved. Today, bread is more or less mold-proofed by the addition of sorbic acid, sodium and calcium propionates, or sodium diacetate, thus rendering ethylene oxide gas obsolete. However, this method of gaseous sterilization has been taken over by the pharmaceutical industry, and today a great many items, including polyethylene and cellophane-wrapped materials, are so treated.

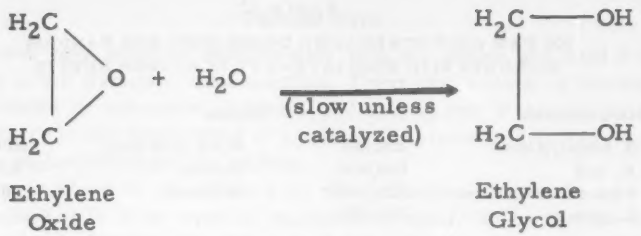


FIGURE 4. Hydrolysis of ethylene oxide.

The first reference to the antibacterial properties of ethylene oxide vapors appeared in a patent filed in 1929, in which it was claimed that insect pests and gems of all kinds are killed by alkylene oxides in conjunction with carbon dioxide.[12] The patent is interesting because, in addition to the broadness of the claims, the theory as to the mechanism of action is presented: that the gas in the presence of moisture is converted to ethylene glycol, and that this change is necessary to achieve sterilization.

Ethylene oxide is capable of reaction with compounds having a labile hydrogen atom, and it reacts with such substances as water, most alcohols, amines, and organic mineral acids. At ordinary temperatures it is a colorless gas and a colorless liquid at temperature below 10.7° C., which is its boiling point. It forms an explosive mixture with air in all proportions from 3 to 80 per cent by volume. This explosion hazard is eliminated when the vapor is mixed in proper proportion with certain gases. Mixtures containing 10 per cent ethylene oxide and 90 per cent carbon dioxide or 11 per cent ethylene oxide and 89 per cent halogenated hydrocarbons are now available for sterilizing purposes without forming an explosive mixture with air. Small quantities of liquid ethylene oxide can be stored in a dry-ice chest provided that the containers are properly sealed. Under no circumstances should the gas be stored in an electric refrigerator, since vapor escaping from the container may form an explosive mixture that could be set off by the motor.

Cases of accidental blistering of the skin due to exposure to ethylene oxide have been reported. Very bad burns have occurred when shoes, clothing, and rubber shoes were worn by laboratory workers immediately after sterilization.[13] Apparently the gas was absorbed by these materials and then diffused out against the skin.

The sterilizing properties of this versatile substance are not confined solely to the gas. In the liquid state it has been used successfully to sterilize such diverse items as culture media, animal feeds, fluid milk, and calf-lymph vaccinia, to mention only a few. In our own laboratories we were able to sterilize two preparations that cannot be sterilized by conventional methods without some deleterious effect. One of these preparations is a highly viscous, heat-labile preparation that,

because of its high ethyl cellulose content, is virtually impossible to sterile-filter. While not overly surprised, we were pleased to find that this product, intended for intravenous injection, was rendered sterile by the mere addition of 1 per cent, by volume, of liquid ethylene oxide. In the second instance we were able to sterilize a whole mouse homogenate, containing, as we all know, myriads of intestinal and skin bacteria.

We now arrive at that very large and most diversified assortment of substances possessing preservative, antiseptic, and disinfectant properties: the nongaseous compounds. These are, to mention the better known classes, the phenols; the metallic compounds, particularly the mercurials; the halogenated compounds; the esters of parahydroxybenzoic acid; the soaps and synthetic detergents that include the quaternary ammonium compounds such as benzalkonium chloride, cetylpyridinium chloride, and domiphen bromide*; the alkalies, acids, and alcohols; and finally, certain antibiotics.

Of all the various classes of antibacterial substances just mentioned, the quaternary ammonium compounds, in my opinion, stand out most prominently. Unlike the others, this group of compounds exhibits not only remarkable germ-killing activity, but possesses surface-active, detergent, and wetting properties as well.

In 1916, Jacobs[14] at The Rockefeller Institute, New York, N.Y., described a group of approximately 100 quaternary ammonium salts of hexamethylene-tetramine, which had bactericidal properties, but it was not until 1935 that the quaternary ammonium compounds attained prominence as important disinfectants and antiseptics, thanks to the work of Domagk.[15]

These surface-active substances have frequently been designated as cationic detergents. In general, these agents materially lower the surface tension of water and are thus surface-active agents. Surface-active substances may have a wetting action as well as detergent action, although both properties do not necessarily exist in the same compound. Most of the presently available quaternary disinfectants have relatively good wetting action but poor detergency.

All of the quaternary ammonium compounds have the general configuration shown in FIGURE 5 in which X represents a halogen, hydroxyl, or alkoxy radical. These ions satisfy the fifth valence of the nitrogen. They are bound differently from the remainder of the atoms in the molecule in that they assume a negative charge.

Surface-active agents may be classified as nonionic or ionic. The ionic substances may be further separated as cationic, in which the lipophilic or oil-attracting group becomes the positively charge cation, or an anionic, in which the lipophilic group becomes the negatively charged anion.

*The trade name of CIBA Pharmaceutical Products Inc. for domiphen bromide is Bradosol.

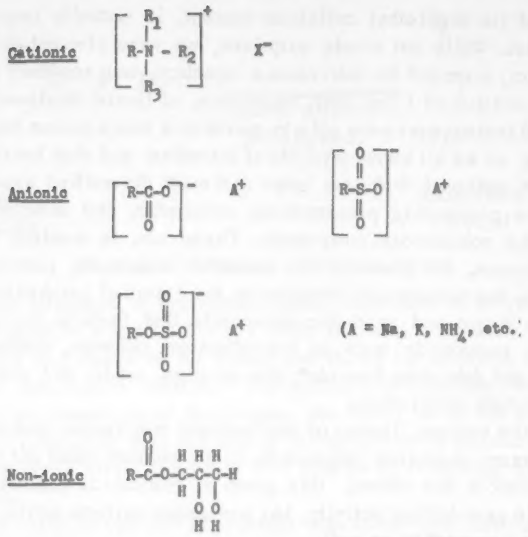
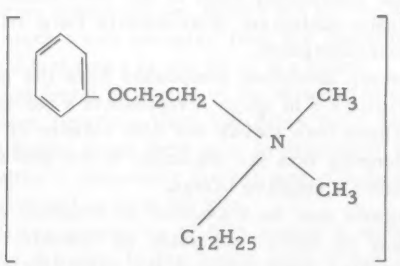


FIGURE 5. Surface-active agents.

Returning to the cationic detergents, that is, the quaternary ammonium compounds, it is clear from the results of a large number of investigators that the general configuration of the molecule is as important for the antibacterial effect as the nature of the individual constituents. It has been postulated that the R groups should consist of one long alkyl or similar group, one short aryl, and two low molecular alkyl radicals, and that the total number of carbon atoms of the long chain should be between 12 to 16. That domiphen bromide fulfills this requirement is shown in FIGURE 6.



Domiphen bromide

(phenoxyethyl-dimethyl-dodecyl-ammo. bromide).

FIGURE 6.

Rather than give a detailed account of the antibacterial activity of quaternary ammonium compounds, suffice it to say that although their activity has been demonstrated principally against vegetative, nonsporulating organisms, some activity of aqueous solutions of these disinfectants has been noted against virulent strains of *Mycobacterium tuberculosis*; however, tinctures of some quaternary ammonium compounds possess reasonably high tuberculocidal activity, as measured by infection-prevention tests. While it is generally known that viruses, in general are somewhat resistant to the action of these agents, it has been shown that appropriate applications of aqueous solutions to wounds containing rabies virus are effective in destroying the virus.

Because of their relatively low toxicity, these compounds have found extensive application as sanitizers in eating and drinking establishments, dairy industries, and various food-processing plants. They are also employed for disinfecting skin and mucous membranes, and also as preservatives for drug formulations.

Other well-known chemical disinfectants include the mercurials, the silver compounds, and the phenolics, to mention only a few, but discussion of them is beyond the scope of this article.

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DIVISION OF PSYCHOLOGY

THE MECHANISM OF SUGAR TRANSPORT INTO THE YEAST CELL*

Vincent P. Cirillo

Department of Oral Microbiology, Seton Hall College of Medicine and Dentistry Jersey City, N.J.

Recent studies using nonmetabolizable sugars have shown that while sugar transport into the yeast cell is a passive process, there is evidence that transport depends upon membrane "carriers" (Cirillo, 1961*a*). Like simple diffusion, sugar transport in yeast does not require metabolic energy and does not occur against a concentration difference. However, unlike simple diffusion, transport has a high Q_{10}, it is stereospecific, it exhibits saturation kinetics, and competition occurs between transported sugars.

These characteristics, described in the experimental section, are discussed in terms of various theories proposed to explain passive but stereospecific transport phenomena.

Methods

The procedures used are essentially those of Burger *et al.* (1959). Commercial baker's yeast (kindly provided by Joel Barkalow of Anheuser-Busch Inc.) was washed by repeated centrifugation in distilled water until the supernatant was clear. The cells were suspended in sugar solutions without buffer at a concentration of 2.0 per cent by volume at 30° C. and incubated on a rotary shaker. At intervals, 5 ml. portions (containing 0.1 ml. of packed cells) were washed by centrifugation with three 5 ml. portions of 0.9 per cent NaCl at 4° C. The washed cells were then extracted with 5 ml. distilled water in a boiling water bath for 20 min.

The several nonmetabolizable sugars were confirmed to be metabolically inert either by incubating with 2.0 per cent yeast suspensions and analyzing the supernatant fluid after various incubation periods or by the Warburg technique.

The cell extracts were analyzed for the transported sugars by the following procedures: reducing sugars, by the Nelson method (Neish, 1952); sorbose, by the alcoholic anthrone method (Wise *et al.*, 1955); and pentoses, by the Bridges method (Bridges, 1952). Sugar concentrations are expressed as milligrams of sugar/milliliter of packed yeast.

In experiments using uranyl nitrate the *p*H was below 3.5; control flasks contained sodium nitrate at the same *p*H.

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Results

Transport of nonmetabolizable sugars. The temperature dependence of L-sorbose uptake is shown in FIGURE 1. After an initial adsorption, which is characteristic for many sugars (see FIGURE 3), uptake is temperature dependent. The transport process is reversible and the rate of efflux into sugar free medium is identical to the rate of influx. At the steady state, sorbose uptake never exceeds the external concentration and is equivalent to distribution into 60 per cent of the cell water. Similar results were reported by Burger *et al.* (1959).

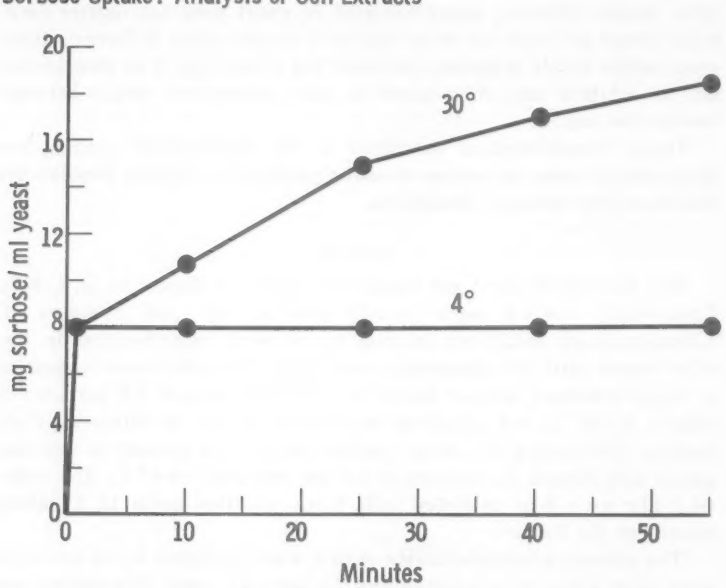

FIGURE 1. L-sorbose uptake. Each point obtained from analysis of hot water extract of 0.1ml. packed cells after 3 washes at 4° C. Incubation mixture: 2.0 per cent (v/v) cell suspension in 5 per cent sorbose shaken on a rotary shaker.

When the rate of uptake at 30° C. is measured as a function of external concentration, saturation kinetics are observed (FIGURE 2). At saturation, the rate of uptake is 2.0 mg./ml. packed yeast/min.

A comparison of the rate of uptake of several nonmetabolizable sugars shows that the transport process is stereospecific. The data of FIGURE 3 show the range in rates of uptake. Also seen is the fact that certain sugars show initial adsorption while others do not. At present no correlation between structure of the sugar and its rate of uptake can be proposed.

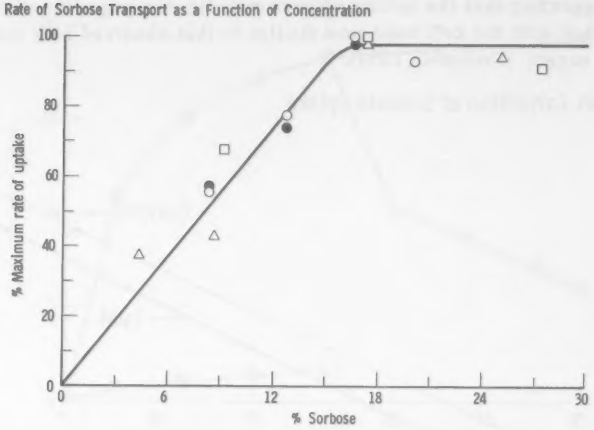

FIGURE 2. Rate of sorbose transport vs extemal concentration. Initial rate of sorbose transport determined as in FIGURE 1 at 30° C.

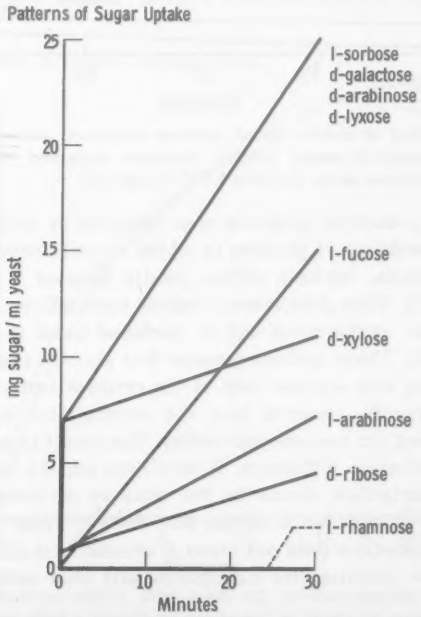

FIGURE 3. Stereospecificity of sugar transport. Sugar content of yeast determined as in FIGURE 1 using 5 per cent sugar, 30° C.

FIGURE 4 shows that the uptake of L-sorbose is inhibited by uranyl ion, suggesting that the uptake of nonmetabolizable sugars involves an interaction with the cell membrane similar to that observed with metabolizable sugars (Rothstein, 1954).

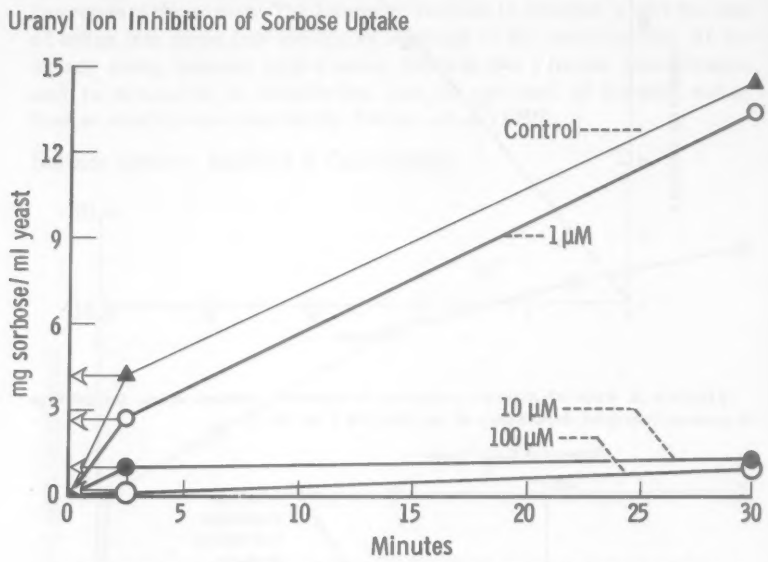

FIGURE 4. Effect of uranyl ion on sorbose transport. Sorbose uptake measured in the presence of uranyl nitrate. Numbers represent μM uranyl ion/ml packed cells. Conditions as in FIGURE 1 30° C, pH 3.0.

Counterflow. L-sorbose uptake is also inhibited by glucose (curve 2, FIGURE 5). In addition, if glucose is added to cells previously equilibrated with sorbose, sorbose efflux results against a concentration gradient (curve 3). This phenomenon, called counterflow, has been described in human erythrocytes and in perfused heart muscle by Park *et al.* (1956,1959). These authors propose that glucose induces counterflow by competing with sorbose only at the external surface of the cell. Because it is rapidly removed from the intracellular environment by metabolism, it does not compete with efflux. The result is sorbose efflux against a concentration difference. If this were so, the rate of sorbose efflux during counterflow should be the same as sorbose efflux into a sugar-free medium; FIGURE 6 shows that the two rates are the same. Furthermore, counterflow does not occur if intracellular glucose is made to accumulate by inhibiting its metabolism with iodo acetic acid (IAA, 10^{-3} *M*).

Of equal interest is the fact that uranyl ion also inhibits counterflow although it does not cause the intracellular accumulation of glucose.

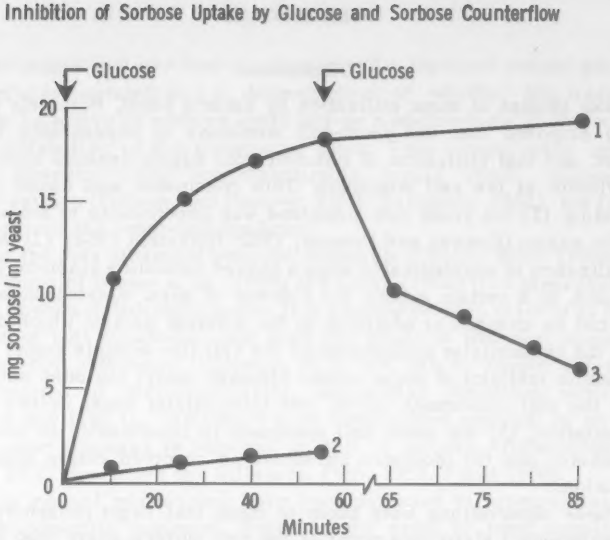

FIGURE 5. Counterflow between L-sorbose and D-glucose. Curve 1: sorbose uptake from 5 per cent sorbose at 40 C. Curve 2: as for curve 1 but 5 per cent glucose present at zero time. Curve 3: 5 per cent glucose (final concentration) added at 60 min.

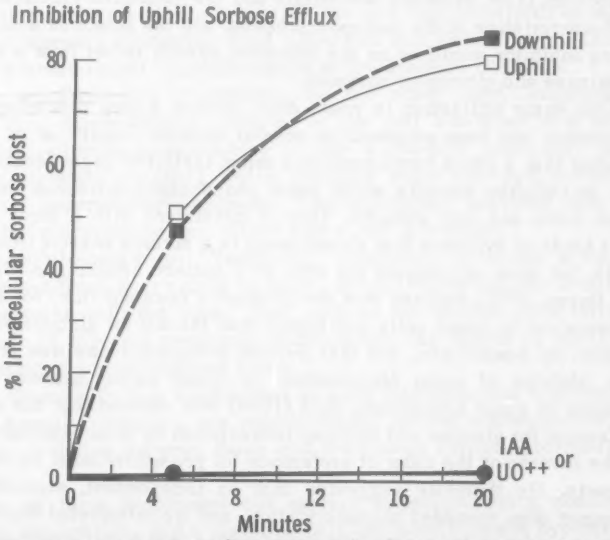

FIGURE 6. Sorbose efflux. One tenth ml. sorbose-loaded cells taken from 5 per cent sorbose after a 60-min-resuspended in distilled water (*downhill*) or a mixture of 5 per cent sorbose plus 5 per cent glucose (*uphill*). The effects of IAA (10^{-3} *M*) and uranyl ion (10 μM/ml. yeast) are shown only for uphill transport.

Discussion

From studies of sugar utilization by baker's yeast, Rothstein (1954, 1956) proposed that the yeast-cell membrane is impermeable to free sugars, and that utilization of metabolizable sugars depends upon phosphorylation at the cell membrane. This conclusion was based on the following: (1) the yeast cell membrane was impermeable to nonmetabolizable sugars (Conway and Downey, 1950; Rothstein, 1954); (2) the rate of utilization of metabolizable sugars obeyed saturation kinetics; (3) the rate and, to a certain extent, the pathway of sugar metabolism was influenced by changes or additions to the external medium which did not alter the intracellular environment of the cell (for example uranyl ion is a specific inhibitor of sugar uptake although uranyl ion does not penetrate the cell membrane); (4) no free intracellular sugar occurs during fermentation; (5) the yeast cell membrane is impermeable to inorganic phosphate; and (6) inorganic phosphate is absorbed during sugar fermentation.

These observations were taken to mean that sugar phosphorylation and subsequent glycolysis occur at the cell surface where they are accessible to influences of the external environment and non-penetrating inhibitors. However, the stereospecific, rate-limiting reaction that occurs at the cell surface could be a transport step preceding intracellular metabolism. If so, substrate specificity and the saturation kinetics would be characteristics of the transport process, and the effect of a nonpenetrating inhibitor would be on the transport system rather than a surface hexokinase and glycolytic enzymes.

That sugar utilization in yeast does involve a step preceding phosphorylation has been proposed by several authors. Derrick *et al.* (1953) reported that a yeast hexokinase antiserum inhibited sugar fermentation only in cell-free extracts while yeast phosphatase antiserum inhibited intact cells and cell extracts. This is consistent with a great deal of other kinds of evidence that phosphatase is a surface enzyme (Rothstein, 1954), but does not support the idea of a surface hexokinase. Blakeley and Boyer, 1955) reported that the Michaelis constant (K_m) for glucose fermentation by intact cells was higher than the K_m for glucose phosphorylation by hexokinase, and that 6-fluoro-6-deoxyglucose was an effective inhibitor of sugar fermentation by intact cells, but was a poor inhibitor of yeast hexokinase. Sols (1956) then showed that the order of preference for glucose and fructose fermentation by intact sauterne yeast is the inverse of the order of preference for phosphorylation by cell-free extracts. He therefore suggested that an independent, stereospecific transport step preceded phosphorylation, and he interpreted Rothstein's data as evidence for a catalytic sugar carrier in the cell membrane. Sols (1961) provided similar evidence that β-galactosides and α-glucosides are transported across the yeast cell membrane by a carrier mechanism before their intracellular hydrolysis. While these studies using metabo-

lizable sugars indicate that a stereospecific transport occurs prior to intracellular metabolism, a determination of whether the transport process is active or passive could not be made because of the subsequent metabolism of the transported sugar. This determination can be made, however, using nonmetabolizable sugars which, contrary to earlier authors (Conway and Downey, 1950; Rothstein, 1954), are transported across the yeast-cell membrane.

From the data presented here and elsewhere (Cirillo, 1959; 1961a and b) and those of Burger *et al.* (1959) and Kotyk (1961) it is clear that the uptake of nonmetabolizable sugars is a passive process since it is independent of cell metabolism and does not result in transport against a concentration difference. However, it is not due to simple diffusion. The features of stereospecificity, competitive inhibition, nonlinear kinetics and high Q_{10} indicate a more complicated process. In this respect sugar transport is identical to that in primate erythrocytes (Le Fevre, 1955; Rosenberg and Wilbrandt, 1955, 1958; Faust 1960).

Three general mechanisms have been proposed to interpret passive but stereospecific transport. Taken in the order of least complexity they are: (1) altered diffusion (Faust, 1960), (2) the membrane-site hypothesis (Le Fevre 1955), and (3) the mobile-carrier hypothesis (Rosenberg and Wilbrandt 1955, 1958).

According to the altered-diffusion hypothesis, pores in the cell membrane communicate with the interior of the cell via convoluted or spiral aqueous channels containing lipid molecules and protein whose spatial relations would impart "specific shape to the aqueous channels."

The membrane-site hypothesis, on the other hand, proposes an enzymelike stereospecific receptor in the cell membrane with which the sugar molecule must combine to form a complex (analogous to an enzyme substrate complex), which mediates sugar transport across an otherwise impermeable membrane. The hypothesis provides that the fixed site be accessible from either side of the membrane.

The mobile-carrier or "ferryboat" hypothesis proposes a mobile rather than a fixed enzymelike receptor, which is alternatively available for complexing with the sugar: first, *only* on the outside, then *only* on the inside of the cell membrane. Furthermore, the carrier is mobile in both combined and uncombined forms.

The altered-diffusion mechanisms and the membrane-site hypothesis, though formally different, are experimentally almost indistinguishable. However, a choice between these and the mobile carrier hypothesis is possible.

While all three hypotheses can explain stereospecificity, nonlinear kinetics, competition, and a high Q_{10}, only the mobile-carrier hypothesis is capable of explaining the phenomenon of counterflow. It is the only hypothesis that can account for an inhibition of influx without an inhibition of efflux. According to either the altered diffusion or membrane

site hypothesis it would be predicted that glucose would block both sorbose influx and efflux equally.

It must be stressed however, that the mobile carrier hypothesis predicts counterflow only if the second sugar is a competitive substrate that can be transported by the carrier. Inhibitors that are not transported (that is, nonpenetrating inhibitors), such as cardiac glycosides in erythrocytes (Le Fevre, 1955) and uranyl ion in yeast (Rothstein, 1954; Cirillo, 1961c) inhibit influx and efflux equally.

These conclusions are summarized schematically in FIGURE 7. External sorbose (S_o) is proposed to combine with unoccupied carrier (X_o) at the external surface of the membrane. The sugar-carrier complex (SX_o) "moves" to the internal surface where it releases intracellular sorbose (Si) and free carrier (Xi). The carrier returns to the external surface occupied or unoccupied depending upon the intracellular sorbose concentration. If glucose is present it competes with sorbose influx. If

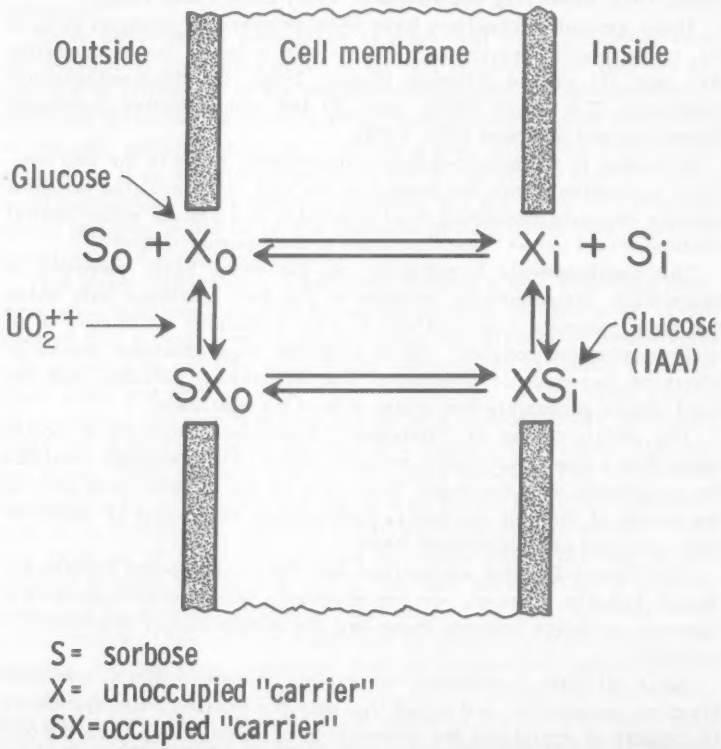

FIGURE 7. Mobile membrane carrier scheme for sugar transport (see text for explanation).

the cell is preloaded with sorbose, glucose addition inhibits only sorbose influx because metabolism removes glucose from the intracellular medium. The result is uphill sorbose efflux or "counterflow." However, if glucose metabolism is blocked by IAA, the accumulated intracellular glucose blocks efflux also, and no counterflow results (this proposal is supported by the fact that sorbose efflux into a sugar-free medium [that is, downhill efflux] is also inhibited when glucose and IAA are present together but is not affected by either glucose or IAA alone.)

Since uranyl ion blocks (1) sorbose influx, (2) downhill efflux, and (3) counterflow, it is proposed that uranyl ion functionally immobilizes the sugar-carrier system, perhaps by combining with the carrier itself, (Cirillo, 1961c).

Summary

Sugar transport into the yeast cell has been studied using nonmetabolizable sugars. While the transport process is passive it has a high Q_{10}, is stereospecific, obeys nonlinear kinetics, and is inhibited by nonpenetrating uranyl ions. Transported sugars show mutual competition and exhibit counterflow. The transport process is interpreted in terms of the mobile carrier or "ferryboat" hypothesis.

Acknowledgment

I express sincere appreciation of the technical assistance provided by Ljubinka Mirov.

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SECTION OF GEOLOGICAL SCIENCES

THE GENESIS OF MINERAL DEPOSITS*

George Mueller
University of Concepción, Concepción, Chile

This paper describes those processes within the earth's crust that produce unusually high, local concentrations of certain elements or compounds, leading thus to the formation of mineral deposits.

The mean abundance of elements thoughout the cosmos is governed by two general trends: (1) it rapidly decreases with increasing atomic weight; and (2) elements with even atomic numbers are somewhat more abundant than their odd numbered neighbors. It should be stressed, however, that the above are but tentative conclusions and that there remain many hitherto unexplained minor irregularities in the composition of what we may term the "universal cocktail" of substance.

The elemental composition of the surface of our planet is, by and large, similar to that of the entire cosmos, but it is relatively impoverished in the lighter elements (He and H in particular) due to their escape from the atmosphere into outer space; moreover the densest metals tend to sink toward the center, forming there the so-called nickel-iron core.

It is interesting to note from TABLE 1 that, as a result of these trends, the earth's crust is composed to an extent of just more than 98 per cent of only 8 major elements, whereas the remaining 84 minor elements, including our most familiar metals in everyday life, figure only in fractional percentages. It should be stressed, however, that the mean cosmic trends in the abundance ratios of elements are still reasonably well preserved on the surface of our planet. Thus, for example, oxygen (atomic weight: 16; atomic number: 8, that is, even) is common, but gold (atomic weight: 197; atomic number: 79, that is, odd) is scarce, not only on earth, but in all the stars that have been thus far spectroscopically analyzed.

The availability of a given metal, nonmetallic element or industrial mineral does not depend solely on its mean abundance, but also on the degree it is able to concentrate within the deposits of mineable dimensions, for example, thousands to millions of tons. The number that indicates how many times a given substance is more concentrated than its average abundance is called the Clarke of concentration. These units cannot be spectacular for the major elements, as deposits of even 100 per cent tenor would represent but a low relative enrichment. It may be seen in TABLE 1, however, that the units for minor elements vary dras-

* This paper is presented in lieu of one entitled "The Chilean Earthquake" presented by the same author at a meeting of the Section on January 3, 1961.

TABLE 1

MODES OF CONCENTRATION OF THE MOST IMPORTANT CHEMICAL ELEMENTS

Element	Mean per cent	Clarkes of concentration in the deposits.	Genetic types of most important deposits; chemical types of the common minerals.
		Major elements.	
O	46.6	0.497-1.1	*Atmosphere:* free. *Oxidate:* dioxide of Mn.
Si	27.72	1.5-1.66	*Placer, pegmatite, hydrothermal:* oxide.
Al	8.13	3.6-4.0	*Hydrolysate:* hydrous oxide.
Fe	5.00	5-14	*Magmatic, hydrothermal, etc:* oxides, etc.
Ca	3.63	8-11	*Precipitate:* carbonate.
Na	2.85	10-14	*Evaporate, fumarole:* chloride, sulphate.
K	2.59	3-8	*Evaporate:* chloride, sulphate.
Mg	2.09	5-13	*Hydrothermal, metamorphic:* carbonate.
		Minor elements: the most important metals	
Ti	0.44	5-55	*Magmatic, pegmatite, placer:* oxides.
Mn	0.100	120-150	*Oxydate, hydrothermal:* oxides.
Cr	0.020	1.200-1.700	*Magmatic:* oxide.
Zn	0.0132	200-2.500	*Hydrothermal:* sulphide, carbonates.
Ni	0.0080	150-400	*Magmatic, hydrothermal:* sulphide.
Cu	0.0070	100-11.000	*Hydrothermal:* sulphides, carbonates, etc.
W	0.0069	30-150	*Hydrothermal:* tungstates.
Sn	0.0040	100-1.000	*Hydrothermal, resistate:* oxide.
Pb	0.0016	2.000-10.000	*Hydrothermal:* sulphide, carbonate
Ga	0.0015	-7	*Hydrothermal:* with sulphides of Zn, Cu.
Mo	0.0015	150-1.200	*Hydrothermal:* sulphide.
Be	0.0006	100-1.000	*Pegmatite:* silicate.
As	0.0005	2.000-30.000	*Hydrothermal, fumarole:* sulphides.
U	0.0004	250-2.000	*Hydrothermal, organic:* oxides, etc.
Hg	0.00005	5.000-160.000	*Hydrothermal:* sulphide.
Bi	0.00002	50.000-1,200.000	*Hydrothermal;* sulphide.
Ag	0.00001	200-300.000	*Hydrothermal:* sulphide, native.
Au	0.0000005	200-60.000	*Hydrothermal, placer:* native, Telleride.
Pt	0.0000005	100-1.500	*Magmatic-placer:* native.
		Minor elements: the most important nonmetals	
H	0.14	78-200	*Hydrosphere:* oxide. *Organic:* hydrocarbons
P	0.118	80-110	*Precipitate, hydrothermal:* phosphates.
S	0.052	300-1.500	*Evaporate, fumarole:* native.
C	0.032	200-3.000	*Metamorphic:* native. *Organic:* coals, etc.
Cl	0.0314	11.500-1.900	*Evaporate, fumarole:* chlorides of alkalies
F	0.0300	100-1.500	*Hydrothermal,* calciumfluoride.
N	0.0046	500-11.640	*Atmosphere:* free. *Evaporates:* nitrates.
B	0.0003	15.000-25.000	*Fumarole, evaporates:* borates.
Br	0.00016	30-100	*Biosphere, hydrosphere:* bromides.
I	0.00003	1.000-30.000	*Evaporate:* iodates, iodides.
A	0.000004	-320.000	*Atmosphere:* free.

tically, ranging for the optimum, presently known top-grade deposits from about 7 (for gallium) up to 1,200,000 (for bismuth). As a general rule, the rate of concentration of a given element increases with the dissimilarity of its chemical properties from the rest, in particular, from the major elements. The actual market value of a metal does not depend directly on its mean abundance, but rather on its Clarkes of concentration in the deposits, the costs of extraction, and the demand. As the result of the above factors, the price of aluminium is about twice that of lead, although the former metal is some 5,000 times more abundant!

In order to reconstruct the diverse modes of concentration of the elements, it is necessary to follow the so-called geochemical cycle: the backbone of the inorganic history of our planet. This initiates, with the intrusion of magma between the rocks, or effusion of lavas from volcanoes to form, after solidification, the coarsely crystalline (slowly cooled) "intrusive rocks" and the fine-grained "effusive rocks," respectively. These are eventually eroded through "atmospheric agencies" over the land surface. The products of erosion, in turn, are redeposited chiefly in the sea as "sedimentary rocks." The latter may become in the course of a large geological time scale of one hundred millions or billions of years, buried to great depth and, as a result of this, heated up, that is, converted to "metamorphic rocks" that may be eventually remolten to new magma, thus completing the cycle.

Each stage of the above geochemical cycle can produce mineral deposits under favorable conditions, as demonstrated below.

Deposits of Magmatic Origin

The composition of the igneous rocks does not deviate drastically from the mean values for the entire earth's crust; they contain about 98 per cent of oxides of the 6 major metals and silicium, which are combined chiefly into silicates, and 2 per cent of minor elements. The dark colored, dense, "basic rocks" (intrusive: dolerite; effusive: basalt) contain, on the average 52 per cent SiO_2; the remainder consists of oxides of major metals and other such components. In the light "acid rocks" (intrusive: granite; effusive: rhyolite) the SiO_2 reaches about 73 per cent, while the composition of the "intermediate rocks" (intrusive: diorite, effusive: andesite) ranges between the above two extremities. In addition to the above 6 most common igneous rocks, a huge number of rarer varieties are distinguishable according to chemical and mineralogical compositions and other criteria. Thus the "ultrabasic rocks," for instance are extremely rich in the oxides of the major metals. As a general trend on the main continental areas, the acid igneous rocks and the types of deposits usually associated with these are more abundant and, to an extent, the continents can be imagined as ships of the light, chiefly granitic rocks, floating on a sea of denser basic magma.

The deposits of direct magmatic origin form, through the crystallization of refractory minerals, from the still liquid magma of the instrusions. These deposits may contain in economic quantities iron and all the other siderophyl (literally "iron-loving") elements that are of similar chemical behavior, that is, producing dense, refractory minerals. These are: nickel, the 6 platinum metals, chromium, and carbon. Basic and ultrabasic rocks in particular are the richest in refractory minerals and, therefore, most of the magmatic deposits are found within these. Random crystallization of refractories within an intrusion leads to a "dispersed" type deposit and, of these, only the famous diamond crystal bearing pipe-shaped intrusions of Kimberley, South Africa are commercially exploitable. However, other disseminated refractories may later concentrate to economic grade deposits through the erosion of the igneous rocks and subsequent redeposition of the grains in "placers," which are described below. If the first crystallized minerals are sufficiently abundant and also considerably denser than the rest of the still liquid magma, then the crystals may sink to the floor of the intrusion, forming there valuable deposits of the "magmatic segregate" type. These deposits, in turn, may eventually outcrop to the surface through uplift of the terrain, accompanied by the erosion of rocks covering the intrusion. The famous iron ores of Kiruna, Sweden, are remarkably pure segregates of the iron oxide, magnetite. All the known deposits of chromium are magmatic segregates as are also some occurences of nickel, copper, titanium, and further deposits of industrial minerals such as emery and garnet. A unique deposit in Disco Bay, Greenland, consists of large blocks of native iron in basalt, a metal utilized by the Eskimos for the fashioning (without melting) of hooks and other small tools.

For a resume of metals and industrial minerals that occur in the magmatic and other types of deposit see TABLE 2. The schematic cross section of the earth crust shown in FIGURE 1 and explained below under *Conclusions*, illustrates the most common forms and settings of all the mineral deposits.

Igneous activity proper terminates with the crystallization of the main mass of the intrusions or effusive lavas. In the course of this there is no abnormal concentration of any constituents and, therefore, no possibility for the formation of deposits. However, it may be mentioned that quick cooling of acid lavas (through cascading into the sea, for example), may lead to the formation of glassy, noncrystallized pumice or perlite: industrial minerals extensively used in the building industry as porous insulators of heat and sound.

Deposits of Postigneous Origin

During and subsequent to the crystallization of a given igneous rock, considerable amounts of water vapors with other volatile constituents are

TABLE 2

GENETIC TYPES OF MINERAL DEPOSITS*

Deposit		M: Metals N: Nonmetals I: Industrial minerals.†
(1) *Magmatic*	(M)	Ti, *Cr, Fe,* Ni, Cu, Pt-metals.
	(I)	*Diamond, emery, garnet, peridot, pumice*
(2) *Postigneous*		
(a) Pegmatite	(M)	*Li, Be,* Al, *Sc,* Ti, *Rb,* Y, *Nb, Cs,* Rare Earth, *Ta*
	(I)	*Felspar, mica, vermiculite, quartz, topaz, aquamarine*
(b) Hydrothermal	(M)	*Mg,* V, Mn, Fe, *Co,* Ni, *Cu, Zn, Ga, Ge, As, Sr, Mo, Ag, Cd, In, Sn, Sb, Te, Ba, W, Re,* Pt-metals, *Au, Hg, Tl, Pb, Bi, U*
	(N)	C, *F,* S, *Se*
	(I)	*Barite, Fluorite, Emerald, Opal, Agate*
(c) Fumarole	(M)	*As, Hg*
	(N)	*B, S,* Cl *Se*
(3) *Sediments*		
(a) Placers	(M)	*Ti,* Fe, *Zr, Pt-metals, Sn, Rare Earth, Hf, Au, Th.*
	(I)	*Quartz sand, diamond, ruby, sapphire*
(b) Hydrolysates	(M)	*Al,* Ni
	(I)	Clays, kaolin
(c) Oxidates	(M)	*Mn,* Fe
(d) Precipitates	(M)	*Ca, Fe,* Cu
	(N)	*P*
	(I)	*Limestone, chalk, chert, flint*
(e) Organic	(M)	V, U
	(N)	H, He, C, P
	(I)	*Peat, coals, anthracite, oil, gas, bitumens, amber*
(f) Evaporate	(M)	Li, *Na, Mg, K,* Sr
	(N)	*B, N, S, Cl,* Br, *I*
	(I)	*Rock salt, gypsum*
(4) *Metamorphic*	(M)	Ti, Mn, Fe, Cu, Zn, Mo, Sn, W, Au
	(N)	C, P
	(I)	*Asbestos, talk, sillimanite,* garnet, corundum
(5) *Hydrosphere*	(N)	*Cl, Br*
(6) *Biosphere*	(N)	Br, Se, J
(7) *Atmosphere*	(N)	*N, O, inert gases*

* The deposits of major importance are italicized

† Industrial minerals are products utilized chiefly in their original state; they include gemstones.

liberated. In case of intrusions, which are by far the more important "parent bodies" of the deposits in question, the minerals may be gradually deposited from the volatiles that ascend and tend to cool within the covering rocks. The form of the deposit would depend on the empty

space available. "Lodes" are mineral filled fissures that may be several miles long and up to 100 feet broad. "Veins" are smaller, mainly vertical mineralized fissures, whereas "flats" are horizontal ones; "stockwork" is an intricate system of veinlets. Less frequently the minerals of the volatiles may crystallize in breccias, irregular caverns, bubbles of lavas, or they may impregnate porous rocks, occasionally to the extent of totally substituting for, or "replacing," their original constituents.

These "postigneous" deposits are, on the whole, characterized with rather restricted dimensions but extremely high concentration rates, from 1,000 to 100,000 or more.

The postigenous deposits may contain the constituents of magma that tend to escape between the broad temperature range of 900° down to 100° C. These can be grouped into two main chemical classes:

(1) the "lithophyl" (that is, "rock-loving") minor elements, which produce a relatively volatile silicate or oxide due to low atomic weight, such as Li, Be, and B, of large ionic radius; Rb, Cs, and U or less well understood reasons, such as, Nb, Ta, and W; and finally, the negative elements, in general.

(2) the "chalcophyl" that is, "copper loving" metals, which form in the magma a minor sulphide phase besides its silicate bulk. These all belong to the side lines of the periodic system, the most important metals of everyday use including Cu, Zn, Ag, Hg, and Pb.

No single postigneous type of deposit contains, in economic concentrations at least, all the elements enumerated above. There are a number of factors that determine which of them would be markedly accumulated in a given deposit and, of these, the pressure and temperature prevailing in the course of condensation of the volatiles are the most important. Using these criteria, we may subdivide the postigneous deposits into several broad groups, as briefly shown below.

Pegmatites. These should be considerated as high pressure, high temperature deposits, which form soon after the solidification of the intrusions, at still elevated temperatures between 500 and 700° C. in usually large irregular fissures or lenses. The latter may often traverse from the intrusion proper to the "roof." There are ample geological evidences to the effect that all the pegmatites formed originally at considerable depth, in the order of many thousands of feet at least and therefore under elevated pressure, and that these pegmatites were exposed by erosion of the covering rocks during later geological epochs.

The pegmatites still contain as a rule, a high proportion of the normal minerals present in igneous rocks but, due to the presence of water, the crystallization is very much slower than in the latter; therefore large crystals form, which in turn can be easily separated from each other either through hand picking or other methods. Thus rough crystals of felspar of the dimensions of a small house have been exploited in several mines in the United States. Another unusually fine-grained constituent

of igneous rocks, is mica, which may reach "books" of up to 15 feet in diameter in some pegmatites from India, whereas perfectly formed, transparent crystals of colorless or smoky quartz the size of a man are not infrequent in deposits from Brazil and Madagascar.

Some pegmatites may contain, in addition, valuable concentrations of the relatively volatile lithophyl elements, such as lithium, beryllium, rubidium, niobium, caesium, and tantalum, chiefly in the form of silicate minerals. Clear varieties of beryl, the silicate of Be, are used as gemstones; the pale blue one is aquamarine, the green one emerald. The latter is found, however, preferentially in the lower temperature, hydrothermal veins. Some other silicates within pegmatites contain, in subeconomic quantities, certain volatile constituents of the magma, such as boron and fluorine, and these often very beautiful minerals: they are occasionally also used as gemstones, such are topaz and tourmaline. All the above elements and minerals are as a general rule somewhat more abundant in acid magmas; therefore, the economically most valuable pegmatites are associated with granitic intrusions.

Hydrothermal deposits. These are also of deep-seated (that is, high-pressure) origin but of low temperature of formation, in contrast to that of the above pegmatites. The evidence of natural thermometers (minerals found in the vein that have melting point, conversion point and other such characteristics within the temperature range in question), indicates a temperature range of formation between 100° and 500° C. The hydrothermal veins are extremely rich in the sulphide ores of the metals from the side lines of the periodic system and, in contrast to the pegmatites, only a few volatile nonchalcophyl elements, such as Fe, Co, W, U, C, F, and P are exploited from them.

The hydrothermal deposits can be subdivided into relatively low, intermediate and high temperature types and, indeed, veins extending to great depths may contain diverse thermal zones, each characterized by a maximum concentration of a given sulphide ore, indicating the gradual cooling of the ascending solutions and the precipitation of progressively more soluble substances. Furthermore, within the intensely mined ore-field in Cornwall, England, transitions from hydrothermal to pegmatitic phases were recorded within the same veins toward greater depth. Careful comparisons of diverse zoned deposits and data obtained through study of the natural thermometers enabled us to establish the approximate order of deposition of metals, with the decreasing temperature of the ascending solutions. An ideal vein would contain the maxima of depositions of the more common metals in the following order:

(pegmatite) - Fe - Sn - W - Cu - Zn - Pb - Ag - Au - Hg

Veins containing the whole or uninterrupted parts of the above thermal sequence are extremely rare. Usually the maxima for one or another metal

is absent, because the mineralizing solutions have been poor in it for hitherto partially understood reasons, as discussed below. Inspite of this factor of uncertainty, the almost ubiquitous presence of some thermal zoning in the major hydrothermal deposits is an important guide for their exploration. Thus the outcrop of a markedly iron-rich vein indicates no hope for more valuable metals to follow beneath, except these or possible pegmatites, whereas a mercury-rich surface zone leaves open the chances for every hydrothermal metal. The above principles apply also for the nonmetallic gangue minerals, which usually accompany the ores. Only their thermal zoning is more diffused. Fluorite and apatite (phosphate of calci um) are rather characteristic for the relatively high temperature veins, whereas barite and celestite (sulphates of barium and strontium, respectively), in addition to calcite and the rather amorphous varieties of silica such as agates and opal are predominant in low temperature deposits. Quartz, including the rarer purple variety, amethyst, is found in most types of veins and, indeed, the familiar white veinlets in most types of veins and, indeed, the familiar white veinlets in the pebbles, which are seen on almost all beaches, are nothing else but the ubiquitous small low temperature hydrothermal quartz veins, which are usually barren of any of the more valuable minerals.

A characteristic feature of many mineral veins is the "comb structure," consisting of a symetrical arrangement of parallel mineral crusts, the eldest, that is, first-deposited mineral species being nearest to the wall rock. Thus, for example, if the order of deposition of three hydrothermal minerals is A – B – C, then the crusts would be positioned within the vein as follows:

(wall-rock) - A - B - C - B - A - (wall-rock)

Som times the central parts, that is, the position of C of the veins, may contain gaps, "vugs" into which often beautiful crystals of the ores and gangues may protrude as crystals of sugar do in liquor-filled chocolates. Many of the most attractive minerals exhibited in museums originate from such vugs in hydrothermal veins. It is interesting to note that the gangues from certain mineralogically famous deposits often reveal characteristic colorations or forms of crystals. As a result of this, an experienced mineralogist can recognize the place of origin of the specimen in question from such noted localities as Kentucky in the United States and Weardale in England; fluorspar and calcite may be found in Muzo, Columbia, which has the highest quality emeralds in addition to many other rare minerals. I observed that the crystals of quartz, calcite, fluorite, and barite from Derbyshire, England, are readily recognized through their elaborate successions of pyritic inclusions deposited in the course of mineralization. Furthermore, sections of crystals originating from each individual lode of the orefield show quite specific patterns

under the microscope, through which the exact mine of origin can be pinpointed.

Most of our metals of everyday life are exclusively or almost exclusively mined from hydrothermal deposits. The major deposits of copper-sulphide ores are stockworks, as at Chuquicamata, Chile. The unusual deposits of native copper from Lake Superior, Canada, are bubble fillings in old basaltic lavas. Sulphides of zinc and lead are usually found together and associated with fluorspar in lodes and veins, often in limestone, as within the orefield in Missouri. Silver is gained mainly as a by-product of lead mines. Tin is found as an oxide in high-temperature veins, whereas gold occurs in the form of native grains and nuggets and in veins that often contain only the precious metal in average quantities of a few parts per million with a quartz gangue. The unique mercury sulphide deposits of Almaden, Spain, often average 2 per cent of the metal, representing about 100,000-fold concentration; it is interesting to note in this connection that the heavy chalcophyl metals which are also markedly volatile, such as, Hg, Bi, and Sb. These metals seem to form the best concentrated hydrothermal deposits. Uranium is found as an oxide in veins or as impregnations of sandstones in Colorado, Canada, and the Congo. A few hydrothermal and pegmatic veins contain also graphite and some interesting bituminous substances, such as, tucholites, which seem to be magmatic volatiles of nonbiological origin. Numerous hydrothermal deposits are economical for sulphides or oxides of iron and, in this connection, it should be noted that this element in question is unique in its potentiality to concentrate in practically every type of deposits due to its rather transitional chemical properties, (TABLE 1).

The composition of a given hydrothermal vein does not solely depend on the pressure and temperature prevailing during its formation. It seems that in addition, the composition of the original volatiles vary in different igneous rocks. This can be ascertained in numerous cases where the original intrusion with which the deposit is associated is sufficiently close to the surface seen in the mines. It seems, for example, that deposits of copper are associated chiefly with basic intrusions, whereas those of tin and uranium are found in veins over granites. Other metals, such as zinc, for example, seem to escape to volatiles from every type of magma. The type of wall rock may also considerably influence the composition and tenor; thus veins traversing sediments are usually the richest in the limestone strata due to precipitation of the metal sulphides with the lime.

It seems that all these factors are still inadequate to explain the remarkable diversity of the hydrothermal deposits. According to the conclusions from my recent work on mineralization of vessicular lavas it appears that, under certain conditions, some supersaturated metal sul-

phides might still escape from the vein without deposition, owing to failure of the formation of crystal nuclei which explains the absence of ores presumably present in every hydrothermal solution (Mueller, 1961).

The sulphide ores within the close-to-surface zones of the hydrothermal deposits convert to hydrated oxides, carbonates, and sulphates through the chemical action of oxygen, water, and carbon dioxide in the atmosphere. These so-called secondary minerals of copper are of blue and green colors; those of uranium, mostly yellow; and the oxides of iron, of course, are brown. The presence of the above vivid coloration of the outcrops of deposits facilitates their detection. The oxidation products, which are more soluble than the primary sulphides, will be gradually washed away by rain water, leaving a partially leached surface zone underlain by a zone of secondary enrichment, in which part of the salts in question became re-deposited. The depths of those two zones of atmospheric effects may vary from a few inches in arctic climates to few hundred feet in humid, tropical climates, although they always stop when the water table is reached. The above irregularities of tenor within the close-to-surface zones renders the assessment of the value of a given prospect difficult without test borings or test pits, although rough information can be obtained through the study of impressions of crystals of the original sulphide ores.

Fumarole deposits. The above described deposits are of deep-seated origin, but the gases from lavas also escape in and near the craters of volcanoes, forming there high temperature, low pressure (with temperatures up to 650° C.) deposits. These are of relatively little economic importance, principally because heavy metal sulphides are absent in quantity, although in the fumaroles of Vesuvius, Italy, for example, scientifically interesting traces of sulphides of zinc, lead, copper, and arsinic have been detected. It seems, however, that the bulk of the heavy metal sulphides dissociate under atmospheric pressure and, as a result of this, the fumarole deposits contain mainly native sulphur, with occasionally admixed selenium. Some fumaroles in California and New Zealand have been worked for sulphide of mercury; rock salt, alum, and sassolite (boric acid) are other products exploited to cover local demands.

Finally, the deposits produced by hot springs can be considered as products of the low-temperature (20 to 100° C.), low-pressure phase of postigneous activity. These might be to a very small scale, exploitable for travertine (a variety of limestone) or silica. It is possible that if a given mineral spring could be followed down to sufficient depth, we should encounter a hydrothermal vein in the process of its mineralization, but thus far this has not been achieved nor, indeed, attempted.

Sediments

Erosion of rocks occurs within the mountainous areas of our globe. It is caused by physical factors such as the friction of running water, wind,

and glacier ice, and the chemical effect of the active constituents in our atmosphere, which are: (1) water; (2) oxygen; (3) carbon dioxide. The products of erosion are transported by rivers and subsequently redeposited as sediments in low-lying basins and, principally, the sea. The process of erosion and sedimentation involves the separation of the original rock into several distinct fractions, some of which may contain concentrations of economic interest. As a general rule, the sedimentary deposits are of very large, close-to-horizontal extention but of low relative concentration rates, which rarely excede 10. For the above reason, they reach economic levels only for the major or the more abundant minor elements with the exception of the "placers." Six types of deposits can be distinguished: placers, hydrolizates, oxidates, precipitates, organic deposits, and evaporates.

Placers. The hard and chemically resistant minerals of both igneous rocks and hydrothermal deposits are carried by the brooks and rivers as sand, grit, or pebbles and are redeposited where the speed of the waters is inadequate for further transport. The resulting sediments are named placers in economic geology, although the geochemical term is "resistate." In mountainous areas the zone of placer deposition may be, on the whole, close to sea shores, whereas within less inclined terrains the waters deposit their transported larger particles farther inland. The most common placer is the familiar deposit of sand, grit, or pebbles of quartz that originates chiefly from quartz grains leached out from granitic rocks and, to a lesser extent, from hydrothermal veins. Heavy black sands of refractory minerals originally dispersed chiefly in basic igneous rocks (see "magmatic" deposits above) often accumulate along sea shores (Florida, India, Scandinavia, Africa, and elsewhere). These deposits may have economic value in that they may include ores of titanium and iron; rare earths, platinum metals, zirconium, and thorium. Of the minerals of hydrothermal origin, only gold and oxide of tin (tinstone) are sufficiently resistant to produce placers along river banks, or more rarely, on the sea shores. Some gold placers may contain the concentrates of huge volumes of auriferous veins eroded throughout many thousands of years; therefore they may be fabulously rich. The discovery of such placers caused the gold rushes of California and Alaska, but as the deposits are relatively shallow river sands, they are quickly exhausted.

Hydrolizates. The large quantities of silicates of aluminium in igneous rocks are hydrolized by the rain water of the atmosphere to fine emulsions of clays, which in turn tend to settle, more seaward from the zone of fall-out of the larger placer grains. The normal clays or the more stratified varieties, the shales, are hydrated silicates of aluminium colored to bluish or brownish shades by oxides of iron. Clays originating from iron-poor granites may eventually lose the bulk of their iron content through prolonged leaching by rain water, particularly if situated in depressions surrounded by unweathered rocks. In this way is obtained

the white china clay or kaolin. Under tropical conditions, on the other hand, the silica may be leached out to a considerable extent, leaving behind relatively pure hydrated oxides of aluminium and iron. The resulting brick-red mineral is bauxite, the only ore of aluminium. Nickel produces occasionally similar types of deposits.

Oxidates. A certain proportion of iron and manganese is liberated after the weathering of rocks in relatively well soluble, two-valent forms, but through prolonged exposure to air, the salts oxidate to the less soluble hydrous oxides. The latter precipitate as brownish emulsions, a familiar sight along the margins of small, marshy flood plains, where the waters of the brooks or rivers spread out and slow down, thus facilitating aeration. Small iron and manganese deposits may eventually form through this process.

Precipitates. The original calcium and magnesium (plus a part of the iron) of the weathering igneous rock is extracted as water-soluble hydrocarbonates through the CO_2 of the atmosphere. These solutions are transported, as a general rule, into the oceans, where the diverse lime-secreting organisms precipitate, principally, calcium carbonate or, occasionally, the double carbonate with magnesium: dolomite. Deposits of carbonates and silicates of iron from Alsace-Lorraine, France, Northhampton, England, and elsewhere are of similar origin. The phosphates of calcium tend to precipitate in large quantities along the continental shelves of the oceans, subjected to upwardflowing currents. The deposits of north Africa, Florida, and other regions are the uplifted product of this process. It is believed that the unique cupriferous slate deposits of Mansfeld, Germany, contain sulphides precipitated by marine organisms. Nearly all the economic "precipitate" type deposits originate from relatively deep sea as when close to the land, they are contaminated with other types of sediments, including placers and hydrolizates. Therefore the presently exploited deposits have been uplifted through tectonic movements and subsequently denuded through erosion; conversely, territories inundated throughout their geological histories by rather deep seas cannot contain precipitate deposits.

Organic deposits. Under the majority of conditions that prevail during sedimentation, the residues of plants and animals are totally destroyed through atmospheric oxidation. However, carbonaceous matter may accumulate in locations where the waters are stagnant and where the little oxygen that enters is inadequate to oxidate the bulk of decaying organic matter. In marshes the residues of dead plants form peat which, when buried throughout geological epochs, undergoes progressive carbonization, converting to lignite, coals, and anthracite in turn. Within closed bays of the sea, sapropel, residues of marine organisms, may accumulate in a similar way. It is believed that the maturing of this latter rather hydrogen-rich sediment should result in the formation of petroleum and natural gas, which, in turn, accumulate in rather porous strata (sandstones

chiefly) and eventually become trapped on top of folds (anticlines) covered by such barriers as impermeable shales. The problem of the origin of petroleum is, however, as yet controversial. Thus the author found that in Derbyshire, England, oil appears wherever coal-bearing shales are traversed by hydrothermal veins, indicating that at least within this locality, oil does not form through direct maturing of a marine sediment but through hydrothermal distillation and hydrogenation of coals, processes that are very similar to the industrial conversion of coals to liquid hydrocarbons. It appears similarly, that a considerable diversity of asphalts and other organic minerals are the result of such natural distillation and cracking of plants in the vicinity of hydrothermal veins and intrusions. Such are, for example, the native paraffin waxes from Poland; elaterite, a rubbery substance from Derbyshire, and olefinite, a hard, natural plastic resin I discovered in certain lead veins from Derbyshire. Amber is a remarkable fossil resin. Some speciments from the main deposits of East Prussia (now the U.S.S.R.) contain perfectly preserved insects and even a lizard that lived about 200 million years ago. The bituminous phases absorb uranium and vanadium of ultimate hydrothermal or sedimentary origin, sometimes producing extensive but low-grade deposits of economic value. Some shales are exploited for uranogenic helium. Finally, guano is a phosphate-rich fertilizer, the residue of birds nesting on oceanic islands, or bats and other cave-dwelling animals.

Evaporates. In the course of erosion, easily soluble salts of the alkali metals, such as magnesium and others, are also leached out from the rocks. Under reasonably humid climates these reach the sea through the the rivers and disperse there, adding to the sea's salinity. Under extremely dry conditions, however, the rather specific "evaporate deposits" may form.

Marine evaporates are produced in drying shallow lagoons that are occasionally replenished with new sea water, as during high tides and storms. As the result of evaporation and replenishment the original salts in the lagoon tend to concentrate and, later on, they begin to crystallize on the bottom, in order of increasing solubility. At first the most insoluble salt, present in quantities in sea water, falls out; this is the sulphate of calcium: gypsum. If the lagoon tends to dry out further through continued evaporation and, possibly, also through gradual severance from the sea due to uplifting, then another layer of the more soluble rock salt falls out on top of the "gypsum zone." Finally, in case of complete dessication, this will be covered by the economically most valuable chlorides and sulphates of potassium and magnesium. The process of evaporation may stop both with the "gypsum" stage or the "rock salt" stage and, indeed, there are but few evaporates that contain the most soluble salts as well. The actual formation of marine evaporates is seen in our time on the Caribbean shores of Colombia, in Karabugaz bay of the Caspian Sea, and other such places. However, the major economic

salt deposits are "fossil," having been buried with other sediments after their formation and subsequently exposed through uplift and erosion. The strata or domelike structures of salt may extend for hundreds of miles and reach thicknesses of several thousands of feet. Such are the deposits in Stassfurt, Germany; in Canada; and elsewhere. Some of the evaporates of Sicily and Louisiana contain exploitable native sulphur that resulted from the reduction of gypsum by microorganisms.

Continental evaporates are formed through the repeated evaporation of salt lakes or periodic desert-lakes without drainage to the sea. The salts are supplied by the waters of the occasional rains, which leach them out from the surrounding rocks, but as these solutions are usually less concentrated than sea water, the resultant crusts of salts rarely exceed a few feet or, indeed, there is only a salt lake present. On the other hand, the deposits are easily exploited because of their superficial character; buried or fossil deposits are unknown, as the thin crusts of salts quickly dissolve through circulating ground waters. The accumulation of certain salts, which are scarce or absent from the sea but relatively abundant within the restricted area of the basin of the particular salt lake in question, may lead to valuable deposits. Such are the numerous soda- and borate-containing lakes or "playas" (crusts) in western parts of the United States, the last-mentioned salt being of ultimate fumarolic origin. The "continental evaporates" are not markedly "zoned" with the exception of the unique nitrate and iodate deposits from northern Chile. There, according to a theory of mine, the "salt pans" or playas formed by the periodic lakes contain only the most abundant salts: gypsum and sodium chloride. However the already concentrated solutions from the periodic or underground lakes moisten the shores through capillary migration, evaporating there to dryness and thus precipitating also the originally diluted salts: the nitrates and iodates in particular. The above process of "two-stage evaporation" can happen only in exceptionally dry basins, with access of solutions strictly from one direction (the direction of the Andes in Chile), because any occasional inflow would wash back and disperse, throughout the salt-pan, the "capillary concentrates."

Metamorphic Deposits

Sediments and other rock types may be subjected to chemical alterations through heating at certain stages of their geological histories; this process is termed metamorphism. If the temperature actually reaches the melting point of the rock, then the magma re-forms, and the geochemical cycle of magma-erosion-sedimentation-metamorphism is thus terminated. Metamorphism is termed regional when it happens through rocks sinking to great depth; "contact" when it is the localized effect of ascending intrusions or lavas.

In general the process of metamorphism does not cause marked con-

centration of elements, but it may produce, through the chemical alteration of constituents of the diverse rocks, valuable industrial minerals. Thus the clays (hydrated silicates of aluminium) lose their water and crystallize in the metamorphic schists as refractory aluminium silicates: andalusite, sillimanite, and kyanite. Hydrated aluminium oxide, bauxite, on the other hand, converts to aluminium oxide, corundum, which is found in Burma, Ceylon, and elsewhere in the form of attractively colored gemstones ruby and sapphire. The metamorphism of impure limestones results in the thermal liberation of carbon dioxide and the formation of a number of silicates, of which garnets are of commercial value as abrasives and, occasionally, as gemstones. Coal seams, on the other hand, may carbonize to graphite. Talcum and asbestos form through metamorphism of old basic igneous rocks.

The above-mentioned industrial minerals may reach economic concentrations in both regional and contact metamorphic rocks. In the later case, however, the products of metamorphism may become intermixed with hydrothermal minerals condensed from the volatiles of the intrusion, although major veins that penetrate beyond the usually 10- to 100-foot broad aureole of contact metamorphism are absent. These rather ill-defined deposits of hybrid metamorphic-hydrothermal origin are termed metasomatic by a number of authorities. They may contain most of the sulphide ores, also iron, titanium, and phosphates.

The Hydrosphere

The sea contains a considerable proportion of the soluble salts extracted from the rocks by rain water throughout the long history of our planet, a period of about 2,000 million years. Some of our rock salt is produced commercially through solar evaporation of sea water, and bromine is also industrially extracted from sea water at the rate of 1 lb. per 2,000 gallons.

The Biosphere

Some living organisms concentrate certain elements to an exploitable degree. Thus iodine and bromine is gained from sea weeds. Experiments have been carried out for the extraction of selenium from certain land plants that markedly concentrate this element.

The Atmosphere

Although our atmosphere contains only 23 per cent oxygen, which is about one half of its percentage in the earth's crust, this element is gained from it, due to the fact that it is present in the free form. After the discovery of processes for synthesizing ammonia and other nitrogen-containing compounds from free N_2, the bulk of this element is now also directly gained from the atmosphere. Finally, all the inert gases, such as argon and neon, are produced from the atmosphere with the single

exception of helium, which is extracted from certain uranium-bearing shales.

Conclusions

For the purposes of a brief summary of the diverse processes that may lead to the formation of mineral deposits, inspection of our tables and of the schematic diagram should serve. TABLE 1 summarizes the most relevant geochemical-economic geological data of the more important elements. TABLE 2 gives a list of "metals", "nonmetals" and "industrial minerals" found in the diverse main genetical types of mineral deposits.

FIGURE 1 shows the main processes (in parentheses) and the resulting types of deposits. Processes and deposits of deep-seated origin are shown beneath the indicated land surface; those of atmospheric origin, above.

In FIGURE 1 the most usual settings and forms of magmatic segregates (within the right-hand intrusion), pegmatites (main, central intrusion), and hydrothermal deposits (left-hand intrusion) are shown. The fault on the right-hand side is mineralized; it is a "lode" originating from a deep-seated intrusion, or it is just a line of weakness through which the rocks displaced (the strata on its left-hand side being evidently uplifted), and volatiles escaped from the depth of the earth's crust. Fumarole and hot-spring deposits are situated within and outside the volcanic crater respectively.

To the left of the watershed in FIGURE 1 erosion is illustrated under reasonably humid conditions. The products of weathering from the high-lying terrains are seen being deposited in the most common order; oxidate, placer, biolith, hydrolisate, and precipitate, although it must be stressed (as also illustrated on the diagram), that considerable interlocking and intermixing between the various types of sediments exist in nature. The section between the fault and the right-hand intrusion shows a series of old sediments that have slipped upward along the fault-line and were in part further uplifted through folding: the two main "tectonic agencies." These may contain all or some of the above types of sediments, in their original state, save that the peats become gradually carbonized to lignite (bituminous, nonbituminous) coals and anthracite, when descending to successively older strata; furthermore, oil and gas may be trapped in the folds beneath impermeable strata (shales). The right-hand side portion shows erosion under arid conditions, with the formation of zoned marine and not zoned continental evaporates, further capillary concentrates. An aureole of rather extensive contact metamorphism surrounds the major, central intrusion, whereas the minor two side-intrusions reveal (as usual) no or little effects of contact metamorphism.

It should be stressed that although the above diagram was not constructed after any definite cross section of the earth's crust and, further,

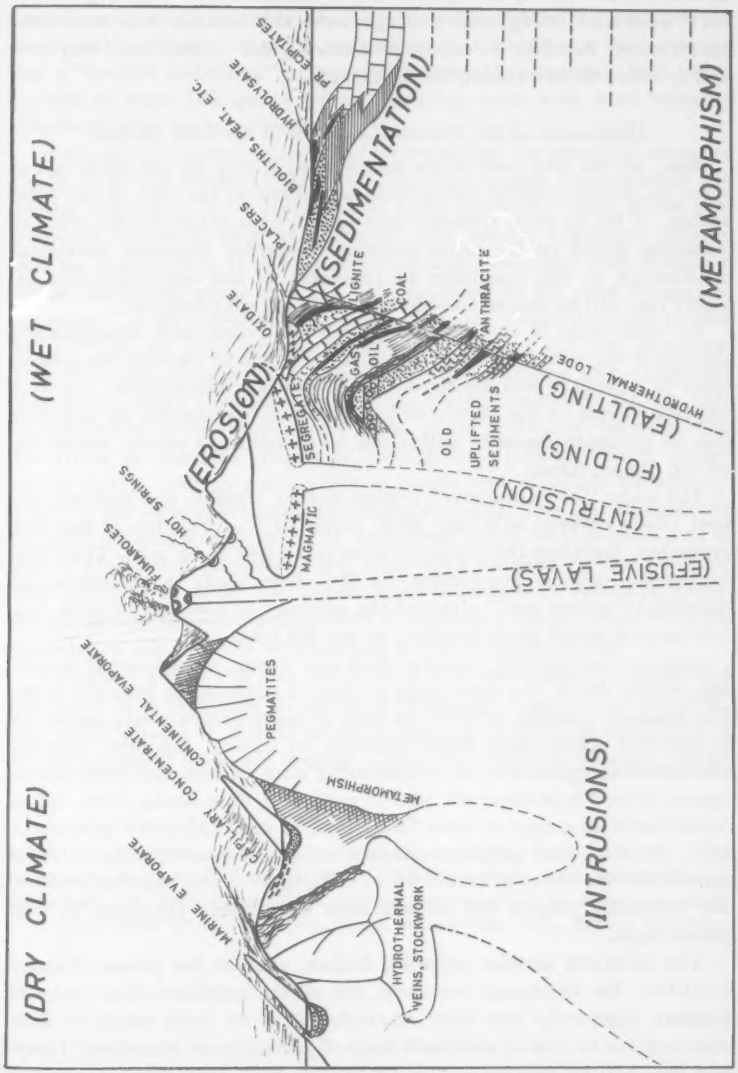
(WET CLIMATE)
(DRY CLIMATE)
(EROSION)
(SEDIMENTATION)
(METAMORPHISM)
(INTRUSIONS)
(FAULTING)
(FOLDING)
(INTRUSION)
(EFFUSIVE LAVAS)
PRECIPITATES
HYDROLYSATE
BIOLITHS, PEAT, ETC.
PLACERS
OXIDATE
SEGREGATE
LIGNITE
COAL
GAS
OIL
ANTHRACITE
HYDROTHERMAL LODE
OLD
UPLIFTED
SEDIMENTS
MAGMATIC
HOT SPRINGS
FUMAROLES
PEGMATITES
METAMORPHISM
CONTINENTAL EVAPORATE
MARINE EVAPORATE
HYDROTHERMAL
VEINS, STOCKWORK

FIGURE 1.

that although the sizes of deposits and vertical elevations are considerably exaggerated, it does not essentially deviate from a possible section of the Rocky Mountains of the United States or the Andes in South America. Through such settings, several intrusions with associated hydrothermal deposits do occur; furthermore, the climate may vary from arid to humid when crossing the watershed.

Discussion of the Mineral Prospects of the Solar System

Now, at the very eve of the space age, it may be not quite out of place to discuss briefly the mineral prospects of the rest of our solar system, if for no other reasons, than to prove (or disprove) the value of reasoning based on the above outlined terrestrial economic geological conclusions in the prediction of prospects of the extraterrestrial deposits that will be encountered by us within the next decades.

To start with, it is unlikely that we shall find such exceptionally high-grade deposits as to repay the transport costs of ore with our present types of rockets, which are driven with chemical combustibles. The most probable advent of the atomic rocket, however, may render the exploitation of top-grade deposits within our solar system a reality within the not too distant future.

The major "outer planets," Jupiter, Saturn, Uranus, and Neptune, are most likely covered with very thick layers of ice, with few if any rock exposures; therefore their mineral prospects seem to be poor. Their predominantly methane atmosphere, on the other hand, is similar to our terrestrial "natural gas," although the economy of transport of such low cost material would prove doubtful, to say the least.

Our two neighboring planets, Mars and Venus, are expected to contain, on the whole, the same range of mineral deposits as does the earth. The apparent scarcity of water on both of these bodies would enable us to prospect almost their entire surfaces for mineral deposits, with the corresponding opportunity of encountering more exceptional-grade occurrences, of the "hydrothermal" type in particular, than on our earth, which is covered to an extent of about 70 per cent by sea. Extremely spectacular gold, platinum, and gemstone placers should be anticipated, as these superficial occurrences should be in a "virgin" state, whereas most of our terrestrial placers had already been extensively plundered by prehistoric man.

The relatively smaller celestial bodies, such as the planets Mercury and Pluto, the asteroids, the moon, and all the satellites (save some of Jupiter), apparently lost their atmospheres at an early epoch of their histories due to lack of sufficient field of gravitational attraction. Therefore they will be found to contain solely magmatic and postigneous type deposits, with the absence of sediments, including placers. Furthermore, it is conceivable that with the decreasing diameter of a celestial body,

its volcanic and postigneous activities would tend to diminish, so that even the latter types of deposits would be rather poorly represented. This argument is further supported by the fact that hitherto no sizable hydrothermal veins or other deposits have been detected amongst the considerable amounts of stony meteorites in our hands; it seems to me that a "random collection" of terrestrial rocks of comparable bulk would contain at least 100 quartz veins, including some with more valuable hydrothermal minerals as well.

In the above connection it should be noted that the generally accepted theory as to meteorites is that they originate through fragmentation and gradual dispersion of the fragments of small celestial bodies of low gravitational cohesion, such as asteroids and comets. Fragments derived from the central core of such a supposed small celestial body contain a native iron-nickel phase that can be considered as the main "magmatic segregate" of all celestial bodies; its existence within the earth is also inferred from the great average density of our planet and from reverberations of waves of earthquakes. The native iron of Disco Bay, Greenland (see above under *Deposits of Magmatic Origin*) seems to be the only representative of this deep-seated phase on the surface of the earth. The meteorites in question consist of nothing less than of "ready made" nickel steels, with as much platinum metals and diamonds as are contained in the most spectacular terrestrial deposits. The famous meteorite crater in Arizona was produced in prehistoric times through an impact of such a nickel-iron fragment, which must have weighed several thousand tons. There is no doubt that a great potential wealth is spread in space, particularly in nickel-iron fragments of dispersed comets; their possible exploitation may prove to be a problem for the imminent future.

The chief purpose of this paper is to give the reader a concise and panoramic view regarding the modes of formation of our mineral deposits. The great volume of details of the processes involved is described in the text-books of economic geology (Lindgren, 1933 and Bateman, 1952).

References

LINDGREN, W. 1933. Mineral Deposits. McGraw-Hill, New York, N.Y.

BATEMAN, A. M. 1952. Economic Mineral Deposits. Wiley. New York, N.Y.

MUELLER, G. 1961. Probability seeding mineralization in vessicular lavas from Chile. 20th Intern. Geol. Congr. Mexico City, D.F., Mexico. In press.

CONFERENCES HELD

DIVISION OF ANTHROPOLOGY

ANTHROPOLOGY AND AFRICA TODAY

Monday, May 1
Tuesday, May 2, and
Wednesday, May 3, 1961

Conference Cochairmen
Ethel Boissevain, Hunter College
New York, N. Y.
Francis P. Conant, University of Massachusetts
Amherst, Mass.
Elliott P. Skinner, New York University
New York, N. Y.

MONDAY, MAY 1, 1961

PHYSICAL ANTHROPOLOGY

Session Chairman: Harry L. Shapiro
American Museum of Natural History New York, N. Y.

9:00 A.M. –

Greetings from the Academy – Ethel Boissevain, Chairman, Division of Anthropology, The New York Academy of Sciences; Hunter College, New York, N. Y.

"The Evidence for Man's Origin in Africa" – L. S. B. Leakey, The Coryndon Museum, Nairobi, Kenya

"Genetics, Morphology, and Taxonomy of the Races of Africa" – L. Oschinsky, Human History Branch, National Museum, Ottawa, Ont., Canada

Discussants: John Buettner-Janusch, Yale University, New Haven, Conn.
Loren C. Eiseley, University of Pennsylvania, Philadelphia, Pa.
Ralph Solecki, Columbia University, New York, N. Y.

PREHISTORY AND HISTORY

Session Chairman: L. S. B. Leakey
The Coryndon Museum, Nairobi, Kenya

2:00 P.M. –

"Contemporary Communities and Abandoned Settlement Sites" – Francis P. Conant, University of Massachusetts, Amherst, Mass.

"Problems in the Reconstruction of African History" – G. P. Murdock, University of Pittsburgh, Pittsburgh, Pa.

Discussants: Warren D'Azevedo, University of Utah, Salt Lake City, Utah
W. A. Fairservis, Jr., American Museum of Natural History, New York, N. Y.

7:00 P.M. –

AFTER-DINNER ADDRESS
"Anthropologists and Africa"
Melville J. Herskovits
Northwestern University, Evanston, Ill.

TUESDAY, MAY 2

ETHNOLOGY AND LINGUISTICS

Session Chairman: Elliott P. Skinner
New York University, New York, N. Y.

9:00 A.M. –

"Material Culture and Ecological Adaptation" – Wm. Bascom, University of California, Berkeley, Calif.

"Problems of Ethnology in Contemporary Africa" – Wm. Schwab, Temple University, Philadelphia, Pa.

"Linguistics as a Tool in African Studies" – Roger W. Westcott, Michigan State University, East Lansing, Mich.

Discussants: Harold Gunn, Lincoln University, Lincoln University, Pa.
Grace Harris, Brandeis University, Waltham, Mass.
Paul Mercier, Musee de l'Homme, Paris, France

PROBLEMS OF FIELD WORK TECHNIQUE

Session Chairman: William Schwab
Temple University, Philadelphia, Pa.

2:00 P.M. –

"Studying Child Rearing and Personality Development in an East African Community" – Robert A. LeVine and Barbara LeVine, University of Chicago, Chicago, Ill.

"Adaptations of Anthropological Techniques to New Social Situations in Africa" – Paul Mercier, Musée de l'Homme, Paris, France

"The Training of American Anthropologists as Africanists" – Igor Kopytoff, Brown University, Providence, R. I.

Discussants: Harold Conklin, Columbia University, New York, N. Y.
Marvin Harris, Columbia University, New York, N. Y.
Hortense Powdermaker, Queens College, Flushing, N. Y.

WEDNESDAY, MAY 3

INSTITUTIONAL CHANGE

Session Chairman: Hugh Smythe
Brooklyn College, Brooklyn, N. Y.

9:00 A.M. –

"Family Change in Contemporary Africa" – Elizabeth Colson, Brandeis University, Waltham, Mass.

"Economic Changes in Indigenous Institutions" – Council Taylor, University of California, Berkeley, Calif.

Discussants: Neville Dyson-Hudson, University of Khartoum, Sudan
Alfred Harris, Brandeis University, Waltham, Mass.

ARTS AND IDEOLOGIES

Session Chairman: Wm. Bascom
University of California, Berkeley, Calif.

2:00 P.M.

"The Arts and Their Changing Social Function" – Roy Sieber, Iowa State University, Ames, Iowa

"Diffusion of Islamic Ideology" – Elliott P. Skinner, New York University, New York, N. Y.

"Changing Concepts of the Self and the Supernatural" – A. Vilakazi, Hartford Theological Seminary, Hartford, Conn.

Discussants: Harold Gunn, Lincoln University, Lincoln University, Pa.
Paul Mercier, Musée de l'Homme, Paris, France
Willard Rhodes, Columbia University, New York, N. Y.
Paul Wingert, Columbia University, New York, N. Y.

DIVISION OF ANTHROPOLOGY

Ethel Boissevain
Chairman

Robert Heckel
Vice-Chairman

SECTION OF BIOLOGICAL AND MEDICAL SCIENCES AND DIVISION OF MATHEMATICS

MATHEMATICAL THEORIES OF BIOLOGICAL PHENOMENA

Monday, May 8
Tuesday, May 9 and
Wednesday, May 10, 1961

Conference Chairman: N. Rashevsky
The University of Chicago, Chicago, Ill.

MONDAY, MAY 8, 1961

Session Chairman: I. Newton Kugelmass
Consultant to the Departments of Health and Hospitals, New York, N. Y.

9:00 A.M. –
Greetings from the Academy – Charles Noback, Chairman, Section of Biological and Medical Sciences, The New York Academy of Sciences, New York, N.Y.; College of Physicians and Surgeons, Columbia University, New York, N. Y.

Opening Remarks – N. Rashevsky, The University of Chicago, Chicago, Ill.

"Mathematical Theory of Reaction Rates" – A. F. Bartholomay, Harvard Medical School, Boston, Mass.

"Applications of Transfer Functions in Pharmacology" – G. Segre, University of Turin, Turin, Italy.

Session Chairman: Herman Branson
Howard University, Washington, D. C.

2:00 P.M. –
"Theory of Lung Functions" – J. G. Defares, University of Leiden, Leiden, The Netherlands.

"Blood Pressure and the Cardiovascular System" – S. Roston, University of Louisville Medical School, Louisville, Ky.

TUESDAY, MAY 9, 1961

Session Chairman: Henry Quastler
Brookhaven National Laboratory, Upton, N. Y.

9:00 A.M. –

"Gibbs Ensembles and Biological Ensembles" – E. H. Kerner, University of Buffalo, Buffalo, N. Y.

"Stochastic Theory of Mortality" – G. Sacher and E. Trucco, Argonne National Laboratory, Argonne, Ill.

Session Chairman: J. H. Woodger
University of London, London, England

2:00 P.M. –

"Theoretical Considerations of Cellular Proliferation as Studied by Cell Labeling Processes" – D. A. Rigas, University of Oregon Medical School, Portland, Ore.

"Electronic Aspects of Quantum Biology" – G. Karreman, Eastern Pennsylvania Psychiatric Institute, Philadelphia, Pa.

WEDNESDAY, MAY 10, 1961

Session Chairman: John Z. Hearon
National Institutes of Health, Bethesda, Md.

9:00 A.M. –

"Mathematical Theory of the Central Nervous System" – H. D. Landahl, The University of Chicago, Chicago, Ill.

"Theory of Physiological Properties of Dendrites" – Wilfrid Rall, National Institutes of Health, Bethesda, Md.

Session Chairman: H. L. Lucas
Institute of Statistics, State College Section, Raleigh, N. C.

2:00 P.M.

"Axiomatization of Biology" – J. H. Woodger, University of London, London, England.

"Mathematical Foundations of General Biology" – N. Rashevsky, The University of Chicago, Chicago, Ill.

SECTION OF BIOLOGICAL AND MEDICAL SCIENCES

Charles Noback
Chairman

Preston L. Perlman
Vice-Chairman

DIVISION OF MATHEMATICS

Bradford F. Hadnot
Chairman

Mary P. Dolciani
Vice-Chairman

DIVISION OF PSYCHOLOGY

FUNDAMENTALS OF PSYCHOLOGY: THE PSYCHOLOGY OF THE SELF

Thursday, May 11, and
Friday, May 12, 1961

Conference Chairman

Muzafer Sherif, University of Oklahoma
Norman, Okla.

Organizing Cochairmen

Ernest Harms, Grand Central Hospital
New York, N. Y.

and

Margaret E. Tresselt, New York University
New York, N. Y.

THURSDAY, MAY 11, 1961

THE DEVELOPMENT OF THE SELF

Session Chairman: William C. H. Prentice
Swarthmore College, Swarthmore, Pa.

9:00 A.M. –
Greetings from the Academy – Louis W. Max, *Chairman,* Division of Psychology, The New York Academy of Sciences, New York, N. Y.

Introductory Remarks – Ernest Harms, Grand Central Hospital, New York, N. Y.

"The Neurological Basis of the Development of the Self" – Fred A. Mettler, College of Physicians and Surgeons, Columbia University, New York, N. Y.

"The Genetic Aspect of the Self" – Charlotte Buhler, University of Southern California Medical School, Los Angeles, Calif.

"The Behavioral Aspect of the Self" – E. Joseph Shoben, Jr., Teachers College, Columbia University, New York, N. Y.

THE DYNAMICS OF THE SELF

Session Chairman: Margaret E. Tresselt
New York University, New York, N. Y.

2:00 P.M. –

"Laws of Symbolic Mediation in the Dynamics of Self and Personality" F. S. Rothschild, University of Jerusalem, Israel

"The Self as Person" – William C. H. Prentice, Swarthmore College, Swarthmore, Pa.

"The Self and Reference Groups: Meeting Ground of Individual and Group Approaches" – Muzafer Sherif, University of Oklahoma, Norman, Okla.

FRIDAY, MAY 12, 1961

THE SELF AND WORLD CONCEPTS

Session Chairman: Charlotte Buhler
University of Southern California, Los Angeles, Calif.

9:00 A.M.

"The Self in Existentialism" – Antonia Wenkart, New York University Medical Center, New York, N. Y.

"Freud's Pathography and Psychoanalysis" – George W. Henry, Cornell University Medical College, New York, N. Y.

"The Religious Approach to the Concept of the Self" – Walter Huston Clark, Hartford School of Religious Education, Hartford, Conn.

THE SELF: ABNORMAL AND NORMAL

Session Chairman: Walter Huston Clark
Hartford School of Religious Education, Hartford, Conn.

2:00 P.M. –

"Evaluating Ego Pathology" – Luise Zucker, Postgraduate Center of Psychotherapy, New York, N. Y.

"Reconstitutive Process in the Psychopathology of the Self" – John W. Perry, University of California Medical School, San Francisco, Calif.

"Self-Consistency Theory and Psychotherapy" – Frederick C. Thorne, University of Vermont Medical School, Burlington, Vt.

DIVISION OF PSYCHOLOGY

Louis W. Max
Chairman

George K. Bennett
Vice-Chairman

SECTION OF BIOLOGICAL AND MEDICAL SCIENCES

BLOOD GROUPS IN INFRAHUMAN SPECIES

Monday, May 15, and
Tuesday, May 16, 1961

Conference Cochairmen

Carl Cohen, Battelle Memorial Institute
Columbus, Ohio
and
D. B. Amos, Roswell Park Memorial Institute
Buffalo, N. Y.

MONDAY, MAY 15, 1961

Session Chairman: Alexander S. Wiener
Jewish Hospital of Brooklyn, Brooklyn, N. Y.

9:00 A.M. –
Greetings from the Academy – Charles Noback, *Chairman,* Section of Biological and Medical Sciences, The New York Academy of Sciences, New York, N. Y.; College of Physicians and Surgeons, Columbia University, New York, N. Y.

"The Objectives of the Conference" – Carl Cohen, Battelle Memorial Institute, Columbus, Ohio

"Blood Groups in Rhesus" – Ray D. Owen and Donald R. Anderson, California Institute of Technology, Pasadena, Calif. and School of Aviation Medicine, Brook Air Force Base, Texas

"Antihuman Sera and Primate Erythrocytes" – John Buettner-Janusch, Yale University, New Haven, Conn.

"*In Vivo* and *in Vitro* Studies of the Behavior of Canine Erythorocyte-Isoantibody Systems" – Scott N. Swisher, Laurence E. Young, and Norma Trabold, University of Rochester School of Medicine and Dentistry, Rochester, N. Y.

"Blood Groups in Rabbits" – Carl Cohen, Battelle Memorial Institute, Columbus, Ohio

"Earlier Studies of Blood Groups in the Rat" – Ray D. Owen, California Institute of Technology, Pasadena, Calif.

"Histocompatibility Antigens and Hemagglutinogens in the Rat" – Arthur

E. Bogden and Paul M. Aptekman, The Biochemical Research Foundation, Newark, Del.

"Current Status of Blood Groups in Rats" – Joy Palm, Wistar Institute, Philadelphia, Pa.

Session Chairman: William C. Boyd
Boston University, Boston, Mass.

2:00 P.M. –
"Blood Groups in Mice" – D. Bernard Amos, Roswell Park Memorial Institute, Buffalo, N. Y.

"Relationship Between Histocompatibility Antigens and Hemagglutinogens in the Mouse" – Ross Basch and Chandler A. Stetson, Bellevue Medical Center, New York, N. Y.

"The Use of Isoimmune Sera for Identification of Lymphoid Cells from Blood-Injected Radiation Chimeras" – Joan W. Goodman, Oak Ridge National Laboratory, Oak Ridge, Tenn.

"Blood Types in Some Marine Mammals" – John Cushing, University of California, Santa Barbara, Calif.

"The Demonstration of Blood Groups in Trout and Salmon by Isoimmunization" – George J. Ridgway, U. S. Bureau of Commercial Fisheries, Seattle, Wash.

"Immunogenetic Studies of Amphibians and Reptiles" – William H. Hildemann, University of California, Los Angeles, Calif.

"Studies of the Erythrocytic Antigens in Species and Species Hybrids of Columbidae" – Donald H. Shaw, University of Wisconsin, Madison, Wis.

8:15 P.M. –

OPEN PANEL SESSION

DISCUSSION OF NOMENCLATURE

Session Chairman: Carl Cohen
Battelle Memorial Institute, Columbus, Ohio

TUESDAY, MAY 16, 1961

Session Chairman: M. R. Irwin
University of Wisconsin, Madison, Wis.

9:00 A.M. –
"Current Status of Blood Groups in Poultry" – Douglas Gilmour, University of Cambridge, Cambridge, England

"Additional Blood Group Systems in the Chicken" – W. Elwood Briles, DeKalb Agricultural Association, Inc., DeKalb, Ill.

"The Effect of Parental *B* Locus Genotypes on Multiple Cross Performance in Chickens" – Courtney P. Allen, Hy-Line Poultry Farms, Johnston, Iowa

"Studies on the 'Hi' Agglutinogen in Chickens" – Sam L. Scheinberg and R. P. Reckel, U. S. Department of Agriculture, Beltsville, Md.

"Blood Groups in Pigs" – Erik Andresen, Iowa State University, Ames, Iowa

"Blood Groups in Pigs and a Preliminary Report on Blood Groups in Mink" – Ruth Saison, Ontario Veterinary College, Guelph, Ont., Canada

"Horse Blood Groups and Haemolytic Disease of the Newborn Foal" – David Franks, University of Cambridge, Cambridge, England

Session Chairman: Lloyd C. Ferguson
Michigan State University, East Lansing, Mich.

2:00 P.M. –

"Current Status of Blood Groups in Cattle" – Clyde Stormont, University of California, Davis, Calif.

"The J Substance of Cattle" – William H. Stone, University of Wisconsin Madison, Wis.

"Studies on the Antigenic Factors of the Blood of Aurochs (*Bison bonasus*)" – Janusz Gasparski, Polish Academy of Science, Warsaw, Poland

"Blood Groups in Sheep' – Benjamin A. Rasmusen, University of Illinois, Urbana, Ill.

"Blood Groups in Chimpanzees, Horses, Sheep, Pigs, and Other Species" André Eyquem, Luba Podliachouk, and P. Millot, Institute Pasteur, Paris, France

SECTION OF BIOLOGICAL AND MEDICAL SCIENCES

Charles Noback
Chairman

Preston L. Perlman
Vice-Chairman

THE BIOLOGY OF THE TRACHOMA AGENT

Friday, May 26 and
Saturday, May 27, 1961

Conference Chairman: Francis B. Gordon
Division of Virology, Naval Medical Research Institute
Bethesda, Md.

FRIDAY, MAY 26, 1961

ISOLATION AND CULTURE METHODS

Session Chairman: L. H. Collier
Medical Research Council, Trachoma Research Unit
Lister Institute of Preventive Medicine, London, England

9:00 A.M –
Greetings from the Academy – Preston L. Perlman, *Vice-Chairman,* Section of Biological and Medical Sciences, The New York Academy of Sciences, New York, N. Y.; Schering Corporation, Bloomfield, N. J.

Opening Remarks – Francis B. Gordon, Division of Virology, Naval Medical Research Institute, Bethesda, Md.

The Embryonated Egg as a Culture Medium

"Historical Background and Review of Isolates" – Phillips Thygeson, Department of Opthalmology, University of California School of Medicine, San Francisco, Calif.

"Isolation of Viruses of Trachoma in Chick Embryos" – E. S. Murray, Department of Microbiology, Harvard School of Public Health, Boston, Mass.

"Isolation of Trachoma and Inclusion Conjunctivitis Viruses in the United States" – Lavelle Hanna, University of California School of Medicine, San Francisco, Calif.

"Seasonal Insusceptibility of Eggs" – Ernest Jawetz, University of California School of Medicine, San Francisco, Calif.

Discussants: L. H. Collier, Medical Research Council, Trachoma Research Unit, Lister Institute of Preventive Medicine, London, England.; Emilio Weiss, Division of Virology, Naval Medical Research Institute, Bethesda, Md.

In Vitro Cell Cultures

"Growth Characteristics of Trachoma and Inclusion Blennorrhea Viruses in Cell Cultures" – L. H. Collier, Medical Research Council, Trachoma Research Unit, Lister Institute of Preventive Medicine, London, England

"Cytochemistry of Trachoma Virus Replication in Tissue Culture" – Morris Pollard, Medical Branch, University of Texas, Galveston, Texas

"Correlation Between Morphological and Biochemical Changes and the Appearance of Infectivity in FL Cell Cultures with Trachoma Agent" – H. Bernkopf, Virus Laboratory, Hadassah Medical School, The Hebrew University, Jerusalem, Israel

"Study of a South African Strain of Trachoma Virus in Tissue Culture" J. H. S. Gear, South African Institute for Medical Research, Johannesburg, South Africa

Discussants: Francis B. Gordon, Division of Virology, Naval Medical Research Institute, Bethesda, Md.; J. Earle Officer, Chemical Corps Biological Laboratories, Fort Detrick, Frederick, Md., and Department of Microbiology, University of Chicago, Chicago, Ill.

NATURE OF THE INFECTIOUS PARTICLE AND ITS MODE OF REPRODUCTION

Session Chairman: James W. Moulder
Department of Microbiology, University of Chicago, Chicago, Ill.

2:00 P.M. –

Some Basic Properties of the Psittacosis-Lymphogranuloma Venereum Group of Agents

"Structure and Chemical Composition of Isolated Particles" – James W. Moulder, Department of Microbiology, University of Chicago, Chicago, Ill.

"Developmental Cycle and Reproductive Mechanisms of the Meningopneumonitis Virus in Strain L Cells" – Noboru Higashi, Division of Biophysics, Institute for Virus Research, Kyoto University, Kyoto, Japan

Discussants: Arthur Brown, Chemical Corps Biological Laboratories, Fort Detrick, Frederick, Md.; George P. Manire, Department of Bacteriology, University of North Carolina Medical School, Chapel Hill, N. C.; Yukihiko Mitsui, Department of Opthalmology, Tokushima University School of Medicine, Tokushima, Japan

Morphology and Developmental Cycle of the Trachoma Agent

"Morphology of Trachoma Agent in Conjunctiva and Chicken Embryo" – Yukihiko Mitsui, Masahiro Kajima, Akira Nishimura, and Katsumoto Konishi, Department of Opthalmology, Tokushima University School of Medicine, Tokushima, Japan

"Developmental Cycle of the Trachoma Agent in the Chorio-allantoic Ectoderm" – Jack Litwin, Department of Microbiology, University of Chicago, Chicago, Ill., and Statens Seruminstitut, Copenhagen, Denmark

Discussants: Morris Pollard, Medical Branch, University of Texas, Galveston, Texas; Earl C. Suitor, Jr., Division of Virology, Naval Medical Research Institute, Bethesda, Md.

PRIMATE EXPERIMENTAL HOSTS

Session Chairman: John C. Snyder
Department of Microbiology, Harvard School of Public Health
Boston, Mass.

8:00 P.M. –
"Infection of Rhesus and Cynomolgus Monkeys with Egg-Grown Trachoma and Inclusion Conjunctivitis Viruses" – Phillips Thygeson and Chandler Dawson, Department of Opthalmology, University of California School of Medicine, San Francisco, Calif.

"Trachoma Infection in Taiwan Monkeys, *Macacus cyclopis*" – San-pin Wang and J. Thomas Grayston, United States Naval Medical Research Unit No. 2, Taipei, Taiwan

"Experimental Infection of Baboons with Trachoma and Inclusion Blennorrhea" – L. H. Collier, Medical Research Council, Trachoma Research Unit, Lister Institute of Preventive Medicine, London, England

"Study of a South African Strain of Trachoma Virus in Experimental Animals" – J. H. S. Gear, South African Institute for Medical Research, Johannesburg, South Africa

"Early Limbal and Corneal Changes in Experimental Human Trachoma Induced by Filtrates" – Phillips Thygeson, Department of Opthalmology, University of California School of Medicine, San Francisco, Calif.

"Inoculation of Man with Inclusion Blennorrhea Virus" – Barrie R. Jones, Institute of Opthalmology, University of London, London, England

SATURDAY, MAY 27, 1961

PHYSIOLOGY AND DRUG SUSCEPTIBILITY

Session Chairman: Emilio Weiss
Division of Virology, Naval Medical Research Institute
Bethesda, Md.

9:00 A.M. –
"Enzymatic Activity Associated with the Meningopneumonitis Agent" – Emma G. Allen and Marianna R. Bovarnick, Department of Biology, Long Island University, Brooklyn, N. Y.

"The Role of Folic Acid in the Metabolism of Members of the Psittacosis Group" – Julio I. Colón, Department of Microbiology, University of Chicago, Chicago, Ill., and Chemical Corps Biological Laboratories, Fort Detrick, Frederick, Md.

Discussant: James W. Moulder, Department of Microbiology, University of Chicago, Chicago, Ill.

"Investigation of the Stability of the Trachoma Agent" – Emilio Weiss and Harry R. Dressler, Division of Virology, Naval Medical Research Institute, Bethesda, Md.

Discussant: L. H. Collier, Medical Research Council, Trachoma Research Unit, Lister Institute of Preventive Medicine, London, England

"Drug Susceptibilities of the Psittacosis and Trachoma Agents" –

Francis B. Gordon and Alice L. Ouan, Division of Virology, Naval Medical Research Institute, Bethesda, Md.

Discussant: Otto E. Landman, Chemical Corps Biological Laboratories, Fort Detrick, Frederick, Md.

"Experimental Chemotherapy of Infection with Agents of the Psittacosis, Lymphogranuloma, Trachoma Group" – E. Weston Hurst, Imperial Chemical Industries, Ltd., Macclesfield, England

Discussants: Ernest Jawetz, University of California School of Medicine, San Francisco, Calif.; Paul B. Johnston, Department of Microbiology, The Jefferson Medical College of Philadelphia, Philadelphia, Pa.

IMMUNOLOGIC STUDIES

Session Chairman: Joseph E. Smadel
Laboratory of Virology and Rickettsiology
Division of Biologic Standards, National Institutes of Health
Bethesda, Md.

2:00 P.M. –
"Immunity in Man Resulting from Infection and in Animals from Vaccine" – Karl F. Meyer, University of California School of Medicine, San Francisco, Calif.

Antigens of the Trachoma-Psittacosis Group

"Complement-fixation Reactions, Group and Type, in Trachoma" – Robert L. Woolridge and J. Thomas Grayston, United States Naval Medical Research Unit No. 2, Taipei, Taiwan

Discussants: L. H. Collier, Medical Research Council, Trachoma Research Unit, Lister Institute of Preventive Medicine, London, England.; E. S. Murray, Department of Microbiology, Harvard School of Public Health, Boston, Mass.

"Cell-Wall Antigens from Members of the Psittacosis Group of Organisms" – Martin R. Ross, State Department of Health, Hartford, Conn., and Howard M. Jenkin, Department of Microbiology, University of Chicago, Chicago, Ill. and Chemical Corps Biological Laboratories, Fort Detrick, Frederick, Md.

"Differentiation of Trachoma Strains on Basis of Immunization Against Toxic Death of Mice" – S. D. Bell, Jr., Department of Microbiology, Harvard School of Public Health, Boston, Mass.

Discussants: H. Bernkopf, Virus Laboratory, Hadassah Medical School, The Hebrew University, Jerusalem, Israel; J. Thomas Grayston, United States Naval Medical Research Unit No. 2, Taipei, Taiwan

Vaccines

"Trachoma Vaccine Studies on Taiwan" – J. Thomas Grayston, Robert L. Woolridge, and San-pin Wang, United States Naval Medical Research Unit No. 2, Taipei, Taiwan.

"Attempt to Immunize a Volunteer by Formalin-Inactivated Trachoma Virus" — John D. Snyder, S. D. Bell, Jr., and E. S. Murray, Department of Microbiology, Harvard School of Public Health, Boston, Mass.; Phillips Thygeson, Department of Opthalmology, University of California School of Medicine, San Francisco, Calif.; and N. Haddad, Aramco Trachoma Research Program, Dhahran, Saudi Arabia

Discussant: L. H. Collier, Medical Research Council, Trachoma Research Unit, Lister Institute of Preventive Medicine, London, England

SECTION OF BIOLOGICAL AND MEDICAL SCIENCES

Charles Noback
Chairman

Preston L. Perlman
Vice-Chairman

NEW MEMBERS

Elected May 25, 1961

LIFE

Audus, Leslie John, Ph.D., Plant Physiology. Professor of Botany, Bedford College, University of London, London, England.

Boyer, Joseph Henry, Ph.D., Organic Chemistry. Assistant Program Administrator, Petroleum Research Fund, American Chemical Society, Washington, D.C.

Bradley, Sterling Gaylen, Ph.D., Genetics. Associate Professor of Bacteriology, University of Minnesota, Minneapolis, Minn.

Brosemer, Ronald Webster, Ph.D., Biochemistry. NSF Postdoctoral Fellow, Physiologisch-Chemisches Institut, Marburg, Lahn, Germany.

Cartwright, Leonard C., M.A., Chemistry. Independent Consultant, New York, N.Y.

Gilbert, Philip L., AB., Immunology and Serology. Vice-President, Certified Blood Donor Service, Inc., Jamaica, L.I., N.Y.

Hoffmann-Ostenhof, Otto, Dr.Phil., Biochemistry. Professor of Biochemistry, University of Vienna, Vienna, Austria.

Hu, Shiu-ying, Ph.D., Botany-Flora of China. Botanist, Amold Arboretum, Harvard University, Cambridge, Mass.

Ikejiani, Okechukwu, Sc.D., Microbiology. Medical Consultant, Pfizer International, Lagos, Nigeria.

SUSTAINING

Fusco, L. Donald, M.D., Medicine. Director, Joseph Fusco Memorial Clinic, Phoenix, Ariz.

ACTIVE

Adkins, Paul C., M.D., Thoracic & Cardiovascular Surgery. Associate Professor of Surgery, The George Washington University Hospital, Washington, D.C.

Alford, Theodore Crandall, M.D., Cancer. Assistant Director, Warwick Cancer Clinic, Washington, D.C.

Alvarez-Bravo, Alfonso, M.D., Gynecology. Professor of Gynecology. Post-Graduate Department, University of Mexico School of Medicine, Mexico, D.F., Mexico.

Anderson, Gordon H., M.D., Medicine. Private Practice, Santa Cruz, Calif.

Angers, John W., M.D., Medical. Henry Nias Fellow-3rd year, Hodgkin Disease Laboratories, St. Vincent Hospital, New York, N.Y.

Arias, Rogelio Ernesto, M.D., Obstetrics. Assistant Chief, Gorgas Hospital, Balboa Heights, Canal Zone.

Armington, Robert Lee, M.D., Neurology. Health Commissioner and Private Practice, Anderson, Ind.

Baicy, Edward O., B.S., Molecular. Chief, Nuclear Physics Branch, Ballistic Research Laboratories, Aberdeeen Proving Ground, Md.

Baker, Everett Meade, M.D., Surgery. Associate Professor, University of Pittsburgh, Pittsburgh, Pa.

Baker, William K., Ph.D., Biochemistry. Research Chemist, Abbott Laboratories, North Chicago, Ill.

Baldwin, Francis P., Ph.D., Polymer Chemistry and Physics. Research As-

sociate-Elastomers Research, Esso Research & Engineering Co., Linden, N.J.

Balke, Bruno, M.D., Physiology. Chief, Biodynamics Branch, Civil Aeromedical Research Institute, Oklahoma City, Okla.

Ball, William P., Ph.D., Nuclear and High Energy Physics. Senior Staff Scientist, Hughes Aircraft Co., Culver City, Calif.

Bankowski, Raymond A., Ph.D., Animal Virology. Professor of Veterinary Medicine, University of California, Davis, Calif.

Barch, William E., B.S., Chemistry of Natural Products. Exploratory Research Division, Head, Fleischmann Laboratories, Standard Brands Inc., Stamford, Conn.

Barham, H. N., Ph.D., Starch, Sorghum Grain Utilization. Consultant, Harvest Queen Mill & Elevator Co., Plainview, Texas.

Barkelew, Chandler H., Ph.D., Chemistry. Supervisor-Development, Shell Development Co., Emeryville, Calif.

Barker, James J., D.Eng.Sci., Nuclear Engineering. Associate Professor, Nuclear Engineering, New York University, New York, N.Y.

Berg, Perry, M.D., Medicine. Instructor in Medicine, New York University College of Medicine, New York, N.Y.

Berte, Stephen J., M.D., Pulmonary Diseases. Chief, Pulmonary Disease Service, 2nd General Hospital, APO 180, New York, N.Y.

Bhattacharya, Bhawani P., B.S., Gynecological Cancer. Consultant Obstetrician, The Georgetown Hospital, British Guiana, South America.

Bigorgne, Michael, D.Sci., Metaux carbonyle. Chef de Travaux, Ecole Nationale Supérieure de Chimie, Laboratoire de Chimie minérale, 11 Rue Pierre Curie, Paris, France.

Blaylock, Lynn G., Ph.D., Nutrition of Poultry. Director of Animal Nutrition, Supersweet Feeds, Minneapolis, Minn.

Boeuf, Alfonso Peña, Estructuras constructivas. Presidente de la Real Academia de Ciencias Exactas, Físicas y Naturales de Madrid, Madrid, Spain.

Bonnett, Howard Thompson, Ph.D., Organic Chemistry. Director Data & Information Center, G. D. Searle & Co., Chicago, Ill.

Borys, Michal Wlodzimierz, M.S., Plant Physiology. Assistant, Plant Physiology Department, Rutgers, The State University, New Brunswick, N.J.

Boyer, Clyde I. Jr., VMD, Veterinary. Professor, Department of Pathology and Bacteriology, Cornell University, Ithaca, N.Y.

Boyle, Frank P., Ph.D., Food Chemistry. Director, New Product Development, Dole Corporation, Honolulu, Hawaii.

Brahms, J., Ph.D., Biochemistry. Research Associate, University of Alberta, Canada.

Breen, James L., M.D., Obstetrics and Gynecology. Fellow, Pathology, The Armed Forces Institute of Pathology, Washington, D.C.

Brindley, C. E., M.D., Endocrinology. In charge of medical information, Merck Sharp & Dohme, East Orange, N.J.

Broido, Abraham, Ph.D., Physical Chemistry. Pioneering Research Specialist, U. S. Forest Service, Berkeley, Calif.

Brokke, Mervin E., Ph.D., Agricultural Chemistry. Senior Research Chemist, Stauffer Chemical Co., Richmond, Calif.

Brown, George W. Jr., Ph.D., Biochemistry. Assistant Professor of Physiological Chemistry. University of Wisconsin, Madison, Wis.

Brown, Leon J., M.S., Nuclear Physics. Staff Member and Assistant Group Leader, Los Alamos Scientific Laboratory, Los Alamos, N. Mex.

Brown, Myrtle L., Ph.D., Nutrition. Nutrition Specialist, Human Nutrition Research Division, U.S. Department of Agriculture, Washington, D.C.

Brown, Raymond M., M.D., Psychiatry, Private Practice, Reno, Nev.

Brown, William Emmett, Ph.D., Physical Chemistry. Assistant Manager, Westco Research Division, The Western Corporation of North America, Dallas, Texas.

Brown, William Lee, B.S., Organic Microchemistry. Chief microchemist, Lilly Research Laboratories, Indianapolis, Ind.

Brueckner, Keith A., Ph.D., Physics. Professor of Physics, University of California, La Jolla, Calif.

Bull, Glen C., Preservation and Storage of Fluids. Glen C. Bull and Associates, Washington, D.C.

Bunnell, Raymond H., Ph.D., Biochemistry. Biochemist, Hoffman-La Roche Inc., Nutley, N.J.

Burns, Richard Henry, M.S., Pharmacology. Research Pharmacologist, Eaton Laboratories, Norwich, N.Y.

Bushey, Albert H., Ph.D., Physical and Analytical Chemistry. Consultant Chemical Applications, General Electric Co., Schenectady, N.Y.

Byram, Edward T., B.E., Rocket Astronomy. Head of Section, Upper Air Physics Branch, Naval Research Laboratory, Washington, D.C.

Call, Tracey G., Ph.D., Pharmacology-Pharmacognosy. Pharmacologist Pharmacognosist, World Life Research Institute, Corona, Calif.

Callis, Clayton Fowler, Ph.D., Inorganic Chemistry. Assistant Director of Research, Monsanto Chemical Co., St. Louis, Mo.

Canady, William J., Ph.D., Biophysical Chemistry. Assistant Professor of Biochemistry, West Virginia University, Morgantown, W. Va.

Cannon, Joseph G., Ph.D., Medicinal Chemistry. Associate Professor of Pharmaceutical Chemistry, University of Wisconsin, Madison, Wis.

Cardoso, Donival Macedo, M.D., Biochemistry. General Secretary, Indústria Brasileira de Produtos, Químicos, South America.

Carr, Marvin S., Ph.D., Chemical Engineering. Professor of Chemistry, Eastern Michigan University, Ypsilanti, Mich.

Carson, John F., Ph.D., Organic Chemistry. Supervisor of Research, Western Regional Research Laboratory, Albany, Calif.

Cason, John H., M.S., Analytical Chemistry. Head, Division of Sciences and Engineering, Pueblo College, Pueblo, Colo.

Cassidy, James Edward, Ph.D., Analytical Chemistry. Research Chemist, American Cyanamid Co., Stamford, Conn.

Caswell, Lyman R., Ph.D., Organic Chemistry. Associate Professor of Chemistry, Upper Iowa University, Fayette, Iowa.

Caudmont, John, Linguistics. Professor, The National University, Bogota, Colombia.

Caul, Jean F., Ph.D., Food and Flavor Research. Senior Project Leader, Life Sciences Division, Arthur D. Little, Inc., Cambridge, Mass.

Celentano, Vincent Dominic, Ph.D., Organic Polymers and Solid Propellants. Research Chemist, Aerojet-General Corp., Sacramento, Calif.

Cerny, Lawrence C., Ph.D., Biophysical Chemistry. Associate Professor of Chemistry, Utica College, Utica, N. Y.

Chaberek, Stanley, Ph.D., Chemistry, Senior Staff Member, Technical Operations, Burlington, Mass.

Chang, Tien Sun, Ph.D., Mechanics and Physics. Professor, Virginia Polytechnic Institute, Blacksburg, Va.

Chang, Wen-Hsuan, Ph.D., Organic Synthesis. Research Chemist, Pittsburgh Plate Glass Co., Springdale, Pa.

Chapin, John L., Ph.D., Physiology. Assistant Professor, University of Colorado, Denver, Colo.

Clark, Melville, Jr., Ph.D., Theoretical Physics. Associate Professor of Nuclear Engineering, Massachusetts Institute of Technology. Cambridge, Mass.

Cohen, Arthur Edwin, M.D. Urology. Senior Resident in Urology. Veterans Administration, New Orleans, La.

Cohen, Gerald, Ph.D., Biochemistry, Associate in Biochemistry, Columbia University College of Physicians and Surgeons, New York, N.Y.

Coleman, Samuel C., M.D., Genetic Perspectives. Chairman, Public and Rural Health, City Clinic, Arkansas City, Ark.

Collier, Jack R., Ph.D., Biochemical Embryology. Investigator, Marine Biological Laboratory, Woods Hole, Mass.

Congdon, M. Stanley, Ph.D., Psychology. Technical Advisor, University of Tarpon Springs, Tarpon Springs, Fla.

Connor, John M., M.S., Biomedical Literature. Los Angeles County Medical Association, Los Angeles, Calif.

Coulter, Joseph R. Jr., BS, EE., Instrumentation in the field of microscopic particle counting and size analysis. President, Coulter Electronics, Inc., Chicago, Ill.

Courant, Richard, Ph.D., Mathematics. Professor Emeritus of Mathematics, Institute of Mathematical Sciences, New York, N.Y.

Crow, Alwyn, Sc.D., General Physics. Consultant, Washington, D.C.

Cusic, John W., M.S., Medicinal Chemistry. Assistant to Director of Chemical Research, G. D. Searle & Co., Chicago, Ill.

Cussen, Arthur J., B.A., Infrared. General Manager, Infrared Standards Laboratory, Riverside, Calif.

Czamecki, Reynold B., Ph.D., Microbiology. Assistant Professor of Bacteriology, University of Massachusetts, Amherst, Mass.

Davis, Milton Wickers, Jr., Ph.D., Chemical Engineering. Research Supervisor, Savannah River Plant, Aiken, S.C.

Davis, Ralph A., M.A., Fluorine Chemistry. Research Chemist, Dow Chemical Co., Midland, Mich.

De Benedictis, Giuseppe, M.D., Biological & Medical Sciences. Staff Assistant of Istituto Di Anatomia e Istologia Patalogica Universita, Bari, Italy.

Defares, James George, Ph.D., Physiology. Lecturer, University of Leyden, Leyden, Holland.

Desnuelle, P., Dr. Sci., Biochemistry. Professor of Biochemistry, University of Marseille, Marseille, France.

Dewey, Edward Russell, S.B., Rhythmic Fluctuation. Director, Foundation for the Study of Cycles, Inc., New York, N.Y.

Dieulefait, Carlos E., Statistics. General Adviser, Consejo Federal de Inversiares, Buenos Aires, Argentina.

Dousmanis, George Christos, Ph.D., Physics. Research Physicist, Radio Corporation of America, Princeton, N.J.

Downing, Mancourt, Ph.D., Biochemistry. Assistant Professor of Chemistry, University of Colorado, Boulder, Colo.

Downs, William G., Jr., Ph.D., Medical Biology. Director, Tennessee Polytechnic Institute, Cookeville, Tenn.

Doyle, Charles Donald, Physical Chemistry of Polymers. Plastics Properties Chemist, General Electric Co., Schenectady, N.Y.

Drummond, Alan M., M.D., Psychoanalysis. Private Practice, Falls Church, Va.

Dhysterhuis, E. J., Ph.D., Plant Ecology. Range Conservationist, U. S. Soil Conservation Service, Lincoln, Nebr.

Eidelhoch, Lester P., M.D., General Surgery, Resident Surgeon, Bronx Municipal Hospital, Bronx, N.Y.

Elchlepp, Jane G., Ph.D., Gastrointestinal Diseases. Surgeon, U. S. Public Health Service, Durham, N.C.

Elder, Charles J., Pharmacology. Junior Pharmacologist, Smith, Kline & French Laboratories, Philadelphia, Pa.

Eliot, Theodore Sessinghaus, Ph.D., Anatomy. Associate Professor of Anatomy, University of Colorado, Denver, Colo.

Ellenbogen, William C., M.S., Analytical Chemistry. Head, Research and Development Division, Smith, Kline & French Laboratories, Philadelphia, Pa.

Ellerbrock, Herman H., Jr., M.S., Aeronautical & Astronautical Propulsion, Chief, Shielding & Propellant Systems Heat Transfer Branch, Lewis Research Center, Cleveland, Ohio.

Ellingson, Robert James, Ph.D., Brain Functions. Associate Professor of Medical Psychology, Nebraska Psychiatric Institute, University of Nebraska College of Medicine, Omaha, Nebr.

Essenfeld, Ervin, M.D., Pathology. Resident in Pathology, Presbyterian Hospital, Pittsburgh, Pa.

Evans, Jimmy R., Ph.D., Medical Bacteriology. Research, Walter Reed Institute of Research, Washington, D.C.

Everets, Warren P., Ph.D., Communications Techniques. Vice-President, Enclyclopaedia Britannica Films, Wilmette, Ill.

Ewing, Reid, S.M., Engineering. Vice-President, Kyova Fiber Pipe Co., Ironton, Ohio.

Falk, Charles E., D.Sc., Nuclear Physics. Assistant to the Director, Brookhaven National Laboratory, Upton, L.I., N.Y.

Feghali, Abdo, D.Sc., Pediatrics-Biochemistry. President, The Sick Children's Hospital of Beirut, Beirut, Lebanon.

Feigley, Charles Anderson, M.D., Medicine. Private Practice, Baton Rouge, La.

Feldballe, Sister Mary Elaine, Ph.D., Endocrinology. Associate Professor of Zoology, Edgewood College, Madison, Wis.

Fife, Earl H. Jr., M.S., Immunology. Supervisory Bacteriologist. Walter Reed Army Institute of Research, Washington, D.C.

Fort, Joel, M.D., Psychiatry. Director, Center for Treatment and Education on Alcoholism, Berkeley, Calif.

Fouché, R. F., DMRD, Medical. Radiologist, Cardiac Clinic, University of Capetown, Capetown, South Africa.

Franko, Bernard V., Ph.D., Medical Sciences. Pharmacologist, A. H. Robins Co. Inc., Richmond, Va.

Freda, Vincent J., M.D., Immunoserology in Obstetrics and Gynecology. Instructor, Columbia University, New York, N.Y.

Fuller, Vernon J., Ph.D., Virology. Virologist, United States Public Health Service, Bethesda, Md.

Gast, Joseph H., Sc.D., Biochemistry. Research Professor, University of San Francisco, San Francisco, Calif.

Gast, Paul F., Ph.D., Nuclear Physics. Manager, Physics & Instrument Research & Development Operation, General Electric Co., Richland, Wash.

Gates, John W. Jr., Ph.D., Organic Research. Senior Research Associate, Eastman Kodak Co., Rochester, N.Y.

Gatos, Harry Costa, Ph.D., Chemistry and metallurgy of electronic materials. Associate Head, Solid State Division, M. I. T. Lincoln Laboratory, Lexington, Mass.

Gausebeck, H. B. Synthetic Resins-Elastomers. European Manager, Rockcote

Colour (G.B.) Ltd., London, England.

Gelvin, E. Raymond, M.D., General Surgery. Chief of Staff, Gelvin-Haughey Clinic, Concordia, Kan.

Gillen, H. William, M.D., Neurologic Research. Attending Neurologist, E. J. Meyer Memorial Hospital, Buffalo, N.Y.

Gillette, Horace Primrose Smith, D.P.H., Medicine. Medical Adviser to the Federal Government of the West Indies, St. Augustine, Trinidad, W. I.

Goldman, David Tobias, Ph.D., Nuclear Physics. Theoretical Physicist, Knolls Atomic Power Laboratory, Schenectady, N.Y.

Goldstein, Rose S., A.B., Psychology. Teacher, High School, New York, N.Y.

Grassé, Pierre-Paul, D.Sc., Biologie Generale. Professeur à la Faculté des Sciences de Paris, Directeur du Laboratoire d'Evolution des Etres Organisés, Paris, France.

Greenberg, Daniel H., Ph.D., Nuclear and Radiation Chemistry. Project Leader, U. S. Industrial Chemicals Co., Plainsboro, N.J.

Greenfield, Myrtle, LL.D. Bacteriology. Director Emeritus, New Mexico Public Health Laboratory, Albuquerque, N. Mex.

Griffin, Harriet, Ph.D., Mathematics. Professor of Mathematics, Brooklyn College, Brooklyn, N.Y.

Gröbner, Wolfgang, Professor, Mathematics. Head, Mathematical Department, University of Innsbruck, Innsbruck, Austria.

Guglielmelli, Silvio M., M.D., Internal Medicine. Chief Cardiac Clinic, Lutheran Medical Center, Brooklyn, N.Y.

Halpern, Bernard, Ph.D., Bacteriology. Pamly Research Laboratory, Northwestern University Medical School, Chicago, Ill.

Hammack, William J., M.D., Hematology. Assistant Professor of Medicine, Medical College of Alabama, Birmingham, Ala.

Hartnett, William Edward, Ph.D., Mathematics. Assistant Professor of Mathematics, College of the Holy Cross, Worcester, Mass.

Hartsell, Stanley Eugene, Ph.D., Bacteriology. Professor of Bacteriology, Purdue University, West Lafayette, Ind.

Harvey, John A., Ph.D., Psychopharmacology. Assistant Professor of Psychology, University of Chicago, Chicago, Ill.

Havemann, Robert, Dr.Phil., Physical Chemistry. Director, Physikalisch-Chemisches Institut der Humbolt-Universitat, Berlin, Germany.

Heezen, Bruce C., Ph.D., Geology. Assistant Professor, Columbia University, New York, N.Y.

Heisterkamp, Charles A. III, M.D., Surgery and Immunology. Captain, M.C. U.S. Army, Philadelphia, Pa.

Heringslake, James E., B.S., Pharmacology. Smith, Kline & French Laboratories, Philadelphia, Pa.

Hessel, Donald W., Ph.D., The chemistry of natural products from marine plants and animals. Research chemist, World Life Research Institute, Colton, Calif.

Hill, Peter, Ph.D., Cellular Biochemistry. National Research Council, Ottawa, Ont., Canada.

Hitchens, John T., B.A., Pharmacology. Pharmacologist (Jr), National Drug Research Laboratories, Philadelphia, Pa.

Horen, Arthur, Ph.D., Mineralogy. Director of Raw Materials, U. S. Steel Corporation, New York, N.Y.

Houlton, Harold G., Ph.D., Petrochemicals. Coordinator Petrochemical Development, Ashland Oil & Refining Co., Ashland, Ky.

Howard, Paul L., M.S., Chemical Sciences. Assistant Vice-President in charge

of Technical Field Operations, Yardney Electric Corporation, New York, N.Y.

Hrachovec, Joseph P., Sc.D., Research in Biological and Medical Sciences. Research Fellow in Gerontology, New York University Medical Center, New York, N.Y.

Huang, Chien Li, Ph.D., Metabolism of Phenothiazine Tranquilizers. Chief Research Chemist, Spring Grove State Hospital, Baltimore, Md.

Kaufman, Jess., B.S., Electronics. Product Manager, Hospital and Nursing Home Division Executive, Merrick, L.I., N.Y.

Kawamura, Kenji, Ph.D., Surgery & Orthopedics. Professor in chief of surgery, Kyoto Prefectural University of Medicine, Kyoto, Japan.

Keller, James Allen, A.B., Solid State Physics. Staff Physicist, Green & Simes, Engineers, Cincinnati, Ohio.

Krishna, V. V. Gopala, Ph.D., High Polymers. Consulting Chemist, Andra Pradesh, Southern India.

Lamberg, Stanley Lawrence, B.S., Mitochondrial Physiology. Charlton Research Fellow, Tufts University School of Medicine, Boston, Mass.

Leimena, J., M.D., Internal Medicine. First Deputy Prime Minister of Distribution, Djakarta, Indonesia.

Leo, Micah Wei Ming, Ph.D., Biochemistry. Research Office, Canada Department of Agriculture, Brandon, Man., Canada.

Ley, Dorothy Corinne Hobbs, M.D., Hematology and Cancer Research. Director of Hematology and Cancer Research Laboratory, Toronto, Ont., Canada.

Lieurance, Richard Edward, M.D., Ophthalmology. Chief of Ophthalmology. U.S.N.H., Oakland, Calif.

Ludwig, Herbert, M.D., Internal Medicine. Chief-physician of the 2nd Medical Division, Bürgerspital Basel, Switzerland.

Maliver, Bruce L., Ph.D., Psychology. School Psychologist, New York City Board of Education, Bronx, N.Y.

Mannick, John A., M.D., Homotransplantation. Instructor in Surgery, Medical College of Virginia, Richmond, Va.

Markel, Casper, M.D., Internal Medicine. Assistant Clinical Professor of Medicine, Denver, Colo.

Marso, Ernest H., M.E., Physical Sciences. Chief Engineer, New York, N.Y.

Massart, E. M. Lucien, D.Sc., Biochemistry. Professor, University of Ghent, Ghent, Belgium.

Mattingly, M. Augustine, Ph.D., Biology. N.I.H. Predoctoral Terminal Fellow, Oak Ridge National Laboratory, Oak Ridge, Tenn.

Mirchamsy, H., VMD, Tissue culture and viral diseases. Associate Director of Immunological Department, State Razi Institute, Tehran, Iran.

Moriconi, Emil J., Ph.D., Organic Chemistry. Chairman, Department of Chemistry, Fordham University, New York, N.Y.

Murray, Walter Alexander Jr., M.D., Pediatric Infectious Diseases. Research Fellow, Department of Pediatrics, Ohio State University, Columbus, Ohio.

Neghme, Amador R., M.D., Biological and Medical Sciences. Director, Department of Parasitology, University of Chile, Santiago, Chile.

Noordergraaf, Abraham, Ph.D., Biophysics. Visiting Fellow, University of Pennsylvania, Philadelphia, Pa.

Oettgen, Herbert F., M.D., Cancer Chemotherapy. Research Associate, Sloan-Kettering Institute for Cancer Research, New York, N.Y.

Ogilvie, Colin, M.D., Medicine. Consultant Physician, United Liverpool Hospitals, Liverpool, England.

Papp, Eugene, Ph.D., Veterinary Pathology. Associate Professor of Pathology, School of Veterinary Medicine, Athens, Ga.

Pearincott, Joseph V., Ph.D., Physiology and Biochemistry. Research Associate, New York Medical College, New York, N.Y.

Pfeffer, Richard L., Ph.D., Meteorology & Oceanography, Senior Scientist, Lamont Observatory, Palisades, N.Y.

Pinter, Joyce K., B.A., Preventive Medicine. Research Assistant, to Doctor Walter S. Wood, University of Illinois, Chicago, Ill.

Pittman, Constance S., M.D., Thyroid. Research Fellow in Medicine, Medical College of Alabama, Birmingham, Ala.

Pittman, James A. Jr., M.D., Thyroid Physiology. Assistant Professor of Medicine, University of Alabama Medical Center, Birmingham, Ala.

Pobanz, Donovan Martin, M.D., Medicine. Faculty, Loyola (Stritch) School of Medicine, Chicago, Ill.

Prelog, Vladimir, M.D., Organic Chemistry. Professor of Organic Chemistry, Federal Institute of Technology, Zurich, Switzerland.

Restrepo, Carlos, M.D., Pathology. Pathologist, Carretera Roosevelt, Guatemala, Guatemala, C. A.

Roc, Serge M., M.D., Surgery. Chief Resident in Surgery. Harlem Hospital, New York, N.Y.

Rochow, William F., Ph.D., Plant Virology. Associate Professor of Plant Pathology, Comell University, Ithaca, N.Y.

Roderick, Howard, B.S., Chemicals. President, Miles Chemical Co., Elkhart, Ind.

Roode, Albert G., M.D., Tropical Medicine. Physician-in-Charge, American Mission Hospital, Pibor Post, via Malakal, Sudan, Africa.

Ross, Ann, M.D., Immunology. Instructor in Experimental Pathology, Western Reserve University, Cleveland, Ohio.

Rubinger, Leonard, M.D., Pathology. Research Fellow, University of California Hospital, San Francisco, Calif.

Sanders, Harold George, Ph.D., Agriculture. Chief Scientific Advisor, Ministry of Agriculture, Fisheries and Food, Whitehall Place, London, England.

Savic, Pavle, Dr. H. C. Nuclear Physics. Professor of Physical Chemistry, University of Belgrade, Belgrade, Yugoslavia.

Schilling, Fred J., M.D., Internal Medicine. Medical Director, St. Luke's Hospital, New York, N.Y.

Schulkind, Herbert, B.S.E.E., Medical Electronics. Electronic Engineer at Photovolt, Long Island Medical Research Group, Garden City, N.Y.

Scott, Sheldon Steven, M.S., Psychology. Laboratory Technician, Wyckoff Heights Hospital, Brooklyn, N.Y.

Serge, Giorgio, Ph.D., Pharmacology. Assistant Professor, Department of Pharmacology, University of Torino, Torino, Italy.

Sergio, Avanzini, M.D., Obstetrics and Gynecology. Assistant, Hospital of Busto Arsizio, Busto Arsizio, Italy.

Sills, Richard D., M.D., Internal Medicine. Private Practice, Detroit, Mich.

Smith, Donald G., M.Sc., Organic Chemistry. Research Officer, National Research Council, Halifax, N.S., Canada.

Stambaugh, Ervin L., M.D., Medicine. Associate Surgeon, Beebe Hospital, Lewes, Del.

Svartz, Nanna Charlotta, M.D., Rheumatology and Intestinal Diseases. Vice-President, King Gustaf V's Research Institute, Stockholm, Sweden.

Tambone, John R., M.D., General Practice. Private Practice, Woodstock, Ill.

Taylor, Edward L., M.S., Cellulose. Chemist, Basic Research Laboratory, K.V.P. Sutherland Co., Kalamazoo, Mich.

Thompson, Robert H. S., D.M., Biochemistry. Professor of Chemical Pathology, London University, London, England.

Tio, Aurelio, Civil Engineer, Engineering. Self-Employed, Santurce, Puerto Rico.

Tobias, Milton, M.D., Interaction of Organismal & Environmental Factors in Childhood Development. Integrating Child & Society, Los Angeles, Calif.

Traube, Sylvia Gould, M.D., Psychiatry. Private Practice, New York, N.Y.

Ugo, Marinoni, M.D., Radioisotopi. Ospedale Di Buso Arsizio, Busto Arsizio, Italy.

Upson, Joseph E., Ph.D., Glacial Geology and Hydrology. Research Geologist, U. S. Geological Survey, Mineola, N.Y.

Vander Noot, George W., M.Ed., Animal Nutrition. Professor of Animal Husbandry, Rutgers University, New Brunswick, N.J.

Vincent, Daniel, M.D., Biochemistry. Professor of Faculty of Medicine, University of Toulouse, Toulouse, France.

Wahl, Izaak, Ph.D., Plant Pathology. Associate Professor, Faculty of Agriculture, The Hebrew University, Rehovoth, Israel.

Waterman, Harriet C., Ph.D., Vertebrate Evolution. Professor of Zoology, Wellesley College, Wellesley, Mass.

West, Milton J., B.A., Biochemistry. Vice-President, Pentex Inc., Kankakee, Ill.

Wheatley, William B., Ph.D., Medicinal Chemistry. Assistant to the Scientific Director, Bristol Laboratories, Syracuse, N.Y.

Wiesner, Jerome B., Ph.D., Electrical Engineering. Special Assistant to the President for Science and Technology, Executive Office Building, Washington, D.C.

Wiggers, Aimee L., M.D., Psychiatry. Director of Psychiatry, Bethlehem Children's Home, Staten Island, N.Y.

Williams, Wallace Reid, Ph.D., Lipid Research. Senior Scientist, Smith, Kline & French Laboratories, Philadelphia, Pa.

Winters, William L., M.D., Cardiovascular. Associate in Medicine, Temple University School of Medicine, Philadelphia, Pa.

Yankelowtiz, Sam, Ph.D., Oral Biochemical Research. Research Biochemist, Oral Health Division, Colgate-Palmolive Co., New Brunswick, N.J.

Younes, Mahmoud, B.S.C., Navigation in narrow water ways, Oil. Chairman, Suez Canal Authority, Ismailia, U.A.R.

STUDENT

Bast, Thomas Franklin II, M.S., Mosquito Biology and Ecology. Research Associate in Entomology, Rutgers University, New Brunswick, N.J.

Bergenn, Victor W., M.A., Experimental Psychology. Biometrics Assistant, New York, N.Y.

Bito, Laszlo Z., B.A., Cell Biology. Graduate Student, Columbia University, New York, N.Y.

Bunim, Lesley Schild, B.A., Medicine-Physiology. Senior, Barnard College, New York, N.Y.

Chakrabarti, Siba G., Ph.D., Biochemistry. Research Fellow, Philadelphia General Hospital, Philadelphia, Pa.

Cousineau, Gilles H., M.S., Molecular Biology. Teaching Fellow, New York University, New York, N.Y.

Feldschuh, Joseph, M.D., Endocrinology. Senior Student, New York University Bellevue School of Medicine, New York, N.Y.

Hoynak, Peter X. Jr., M.S., Food Science. Research Assistant, Rutgers, The State University, New Brunswick, N.J.

Hunter, Floyd, M.A., Zoology-Endocrinology. Graduate Student, Teaching Assistant, Rutgers, The State University, New Brunswick, N.J.

Mhatre, Nagesh S., M.S., Biochemistry-Microbiology. Research Assistant, Rutgers, The State University, New Brunswick, N.J.
Pliskin, Robert, Geology. Student, Columbia University, New York, N.Y.
Sanel, Frances Thaw, B.A., Cytology. Predoctoral candidate, Columbia University, New York, N.Y.

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